FIG. 1

Sequence of human APRIL (SEQ ID NOS: 1 and 2)

Human G70 cDNA (SEQ ID NO 1)
Length: 1465 bp

```
   1  GCCAACCTTC CCTCCCCCAA CCCTGGGGCC GCCCCAGGGT TCCTGCGCAC
  51  TGCCTGTTCC TCCTGGGTGT CACTGGCAGC CCTGTCCTTC CTAGAGGGAC
 101  TGGAACCTAA TTCTCCTGAG GCTGAGGGAG GGTGGAGGGT CTCAAGGCAA
 151  CGCTGGCCCC ACGACGGAGT GCCAGGAGCA CTAACAGTAC CCTTAGCTTG
 201  CTTTCCTCCT CCCTCCTTTT TATTTTCAAG TTCCTTTTTA TTTCTCCTTG
 251  CGTAACAACC TTCTTCCCTT CTGCACCACT GCCCGTACCC TTACCCGCCC
 301  CGCCACCTCC TTGCTACCCC ACTCTTGAAA CCACAGCTGT TGGCAGGGTC
 351  CCCAGCTCAT GCCAGCCTCA TCTCCTTTCT TGCTAGCCCC CAAAGGGCCT
 401  CCAGGCAACA TGGGGGGCCC AGTCAGAGAG CCGGCACTCT CAGTTGCCCT
 451  CTGGTTGAGT TGGGGGGCAG CTCTGGGGGC CGTGGCTTGT GCCATGGCTC
 501  TGCTGACCCA ACAAACAGAG CTGCAGAGCC TCAGGAGAGA GGTGAGCCGG
 551  CTGCAGGGGA CAGGAGGCCC CTCCCAGAAT GGGGAAGGGT ATCCCTGGCA
 601  GAGTCTCCCG GAGCAGAGTT CCGATGCCCT GGAAGCCTGG GAGAGTGGGG
 651  AGAGATCCCG GAAAAGGAGA GCAGTGCTCA CCCAAAAACA GAAGAAGCAG
 701  CACTCTGTCC TGCACCTGGT TCCCATTAAC GCCACCTCCA AGGATGACTC
 751  CGATGTGACA GAGGTGATGT GGCAACCAGC TCTTAGGCGT GGGAGAGGCC
 801  TACAGGCCCA AGGATATGGT GTCCGAATCC AGGATGCTGG AGTTTATCTG
 851  CTGTATAGCC AGGTCCTGTT TCAAGACGTG ACTTTCACCA TGGGTCAGGT
 901  GGTGTCTCGA GAAGGCCAAG GAAGGCAGGA GACTCTATTC CGATGTATAA
 951  GAAGTATGCC CTCCCACCCG GACCGGGCCT ACAACAGCTG CTATAGCGCA
1001  GGTGTCTTCC ATTTACACCA AGGGGATATT CTGAGTGTCA TAATTCCCCG
1051  GGCAAGGGCG AAACTTAACC TCTCTCCACA TGGAACCTTC CTGGGGTTTG
1101  TGAAACTGTG ATTGTGTTAT AAAAAGTGGC TCCCAGCTTG GAAGACCAGG
1151  GTGGGTACAT ACTGGAGACA GCCAAGAGCT GAGTATATAA AGGAGAGGGA
1201  ATGTGCAGGA ACAGAGGCGT CTTCCTGGGT TTGGCTCCCC GTTCCTCACT
1251  TTTCCCTTTT CATTCCCACC CCCTAGACTT TGATTTTACG GATATCTTGC
1301  TTCTGTTCCC CATGGAGCTC CGAATTCTTG CGTGTGTGTA GATGAGGGGC
1351  GGGGGACGGG CGCCAGGCAT TGTTCAGACC TGGTCGGGGC CCACTGGAAG
1401  CATCCAGAAC AGCACCACCA TCTAACGGCC GCTCGAGGGA AGCACCCGGC
1451  GGTTTGGGCG AAGTC
```

The proposed transmembrane domains are boxed

human G70 protein sequence (SEQ ID NO 2)

```
  1  MPASSPFLLA PKGPPGNMGG PVREPALSVA LWLSWGAALG AVACAMALLT

 51  QQTELQSLRR EVSRLQGTGG PSQNGEGYPW QSLPEQSSDA LEAWESGERS

101  RKRRAVLTQK QKKQHSVLHL VPINATSKDD SDVTEVMWQP ALRRGRGLQA

151  QGYGVRIQDA GVYLLYSQVL FQDVTFTMGQ VVSREGQGRQ ETLFRCIRSM

201  PSHPDRAYNS CYSAGVFHLH QGDILSVIIP RARAKLNLSP HGTFLGFV
```

FIG. 2A

Sequence of mouse G70 (SEQ ID NOS: 3 and 4)

```
Mouse G70 (SEQ ID NO 3)
   1  CATGCCGAGT GCTTTGTGTG TGTTACCTGC TCTAAGAAGC TGGCTGGGCA
  51  GCGTTTCACC GCTGTGGAGG ACCAGTATTA CTGCGTGGAT TGCTACAAGA
 101  ACTTTGTGGC CAAGAAGTGT GCTGGATGCA AGAACCCCAT CACTGGGTTT
 151  GGTAAAGGCT CCAGTGTGGT GGCCTATGAA GGACAATCCT GGCACGACTA
 201  CTGCTTCCAC TGCAAAAAAT GCTCCGTGAA TCTGGCCAAC AAGCGCTTTG
 251  TATTTCATAA TGAGCAGGTG TATTGCCCTG ACTGTGCCAA AAAGCTGTAA
 301  CTTGACGGCT GCCCTGTCCT TCCTAGATAA TGGCACCAAA TTCTCCTGAG
 351  GCTAGGGGGG AAGGAGTGTC AGAGTGTCAC TAGCTCGACC CTGGGGACAA
 401  GGGGGACTAA TAGTACCCTA GCTTGATTTC TTCCTATTCT CAAGTTCCTT
 451  TTTATTTCTC CCTTGCGTAA CCCGCTCTTC CCTTCTGTGC CTTTGCCTGT
 501  ATTCCCACCC TCCCTGCTAC CTCTTGGCCA CCTCACTTCT GAGACCACAG
 551  CTGTTGGCAG GGTCCCTAGC TCATGCCAGC CTCATCTCCA GGCCACATGG
 601  GGGGCTCAGT CAGAGAGCCA GCCCTTTCGG TTGCTCTTTG GTTGAGTTGG
 651  GGGGCAGTTC TGGGGGCTGT GACTTGTGCT GTCGCACTAC TGATCCAACA
 701  GACAGAGCTG CAAAGCCTAA GGCGGGAGGT GAGCCGGCTG CAGCGGAGTG
 751  GAGGGCCTTC CCAGAAGCAG GGAGAGCGCC CATGGCAGAG CCTCTGGGAG
 801  CAGAGTCCTG ATGTCCTGGA AGCCTGGAAG GATGGGGCGA AATCTCGGAG
 851  AAGGAGAGCA GTACTCACCC AGAAGCACAA GAAGAAGCAC TCAGTCCTGC
 901  ATCTTGTTCC AGTTAACATT ACCTCCAAGG ACTCTGACGT GACAGAGGTG
 951  ATGTGGCAAC CAGTACTTAG GCGTGGGAGA GGCCTGGAGG CCCAGGGAGA
1001  CATTGTACGA GTCTGGGACA CTGGAATTTA TCTGCTCTAT AGTCAGGTCC
1051  TGTTTCATGA TGTGACTTTC ACAATGGGTC AGGTGGTATC TCGGGAAGGA
1101  CAAGGGAGAA GAGAAACTCT ATTCCGATGT ATCAGAAGTA TGCCTTCTGA
1151  TCCTGACCGT GCCTACAATA GCTGCTACAG TGCAGGTGTC TTTCATTTAC
1201  ATCAAGGGGA TATTATCACT GTCAAAATTC CACGGGCAAA CGCAAAACTT
1251  AGCCTTTCTC CGCATGGAAC ATTCCTGGGG TTTGTGAAAC TATGATTGTT
1301  ATAAAGGGGG TGGGGATTTC CCATTCCAAA AACTGGCTAG ACAAAGGACA
1351  AGGAACGGTC AAGAACAGCT CTCCATGGCT TTGCCTTGAC TGTTGTTCCT
1401  CCCTTTGCCT TTCCCGCTCC CACTATCTGG CCTTTGACTC CATGGATATT
1451  AAAAAAGTAG AATATTTTGT GTTTATCTCC CAAAAA
```

FIG. 2B

Mouse G70 Length: 241 (SEQ ID NO 4)

1	MPASSPGHMG	GSVREPALSV	ALWLSWGAVL	GAVTCAVALL	IQQTELQSLR
51	REVSRLQRSG	GPSQKQGERP	WQSLWEQSPD	VLEAWKDGAK	SRRRRAVLTQ
101	KHKKKHSVLH	LVPVNITSKD	SDVTEVMWQP	VLRRGRGLEA	QGDIVRVWDT
151	GIYLLYSQVL	FHDVTFTMGQ	VVSREGQGRR	ETLFRCIRSM	PSDPDRAYNS
201	CYSAGVFHLH	QGDIITVKIP	RANAKLSLSP	HGTFLGFVKL	*

G-70 FLAG des92 (smuG70) Strain #4081 (SEQ ID NO 19):

MDYKDDDDKKHKKKHSVLHLVPVNITSKDSDVTEVMWQPVLRRGRGLEAQGDIVRVWDTGIY
LLYSQVLFHDVTFTMGQVVSREGQGRRETLFRCIRSMPSDPDRAYNSCYSAGVFHLHQGDII
TVKIPRANAKLSLSPHGTFLGFVKL*

FIG. 3

Alignm of human and mouse G70

```
mouse:   1   MPASS----------PGHMGGSVREPALSVALWLSWGAVLGAVTCAVALLIQQTELQSLRR   51
             MPASS          PG+MGG VREPALSVALWLSWGA LGAV CA+ALL QQTELQSLRR
human:   1   MPASSPFLLAPKGPPGNMGGPVREPALSVALWLSWGAALGAVACAMALLTQQTELQSLRR   60

mouse:   52  EVSRLQRSGGPSQKQGERPWQSLWEQSPDVLEAWKDGAKSRRRRAVLTQKHKKKHSVLHL  111
             EVSRLQ +GGPSQ      PWQSL EQS D LEAW+ G +SR+RRAVLTQK KK+HSVLHL
human:   61  EVSRLQGTGGPSQNGEGYPWQSLPEQSSDALEAWESGERSRKRRAVLTQKQKKQHSVLHL  120

mouse:   112 VPVNITSKD-SDVTEVMWQPVLRRGRGLEAQGDIVRVWDTGIYLLYSQVLFHDVTFTMGQ  170
             VP+N TSKD SDVTEVMWQP LRRGRGL+AQG  VR+ D G+YLLYSQVLF DVTFTMGQ
human:   121 VPINATSKDDSDVTEVMWQPALRRGRGLQAQGYGVRIQDAGVYLLYSQVLFQDVTFTMGQ  180

mouse:   171 VVSREGQGRRETLFRCIRSMPSDPDRAYNSCYSAGVFHLHQGDIITVKIPRANAKLSLSP  230
             VVSREGQGR+ETLFRCIRSMPS PDRAYNSCYSAGVFHLHQGDI++V IPRA AKL+LSP
human:   181 VVSREGQGRQETLFRCIRSMPSHPDRAYNSCYSAGVFHLHQGDILSVIIPRARAKLNLSP  240

mouse:   231 HGTFLGFVKL 240
             HGTFLGFVKL
human:   241 HGTFLGFVKL 250
```

FIG. 4A

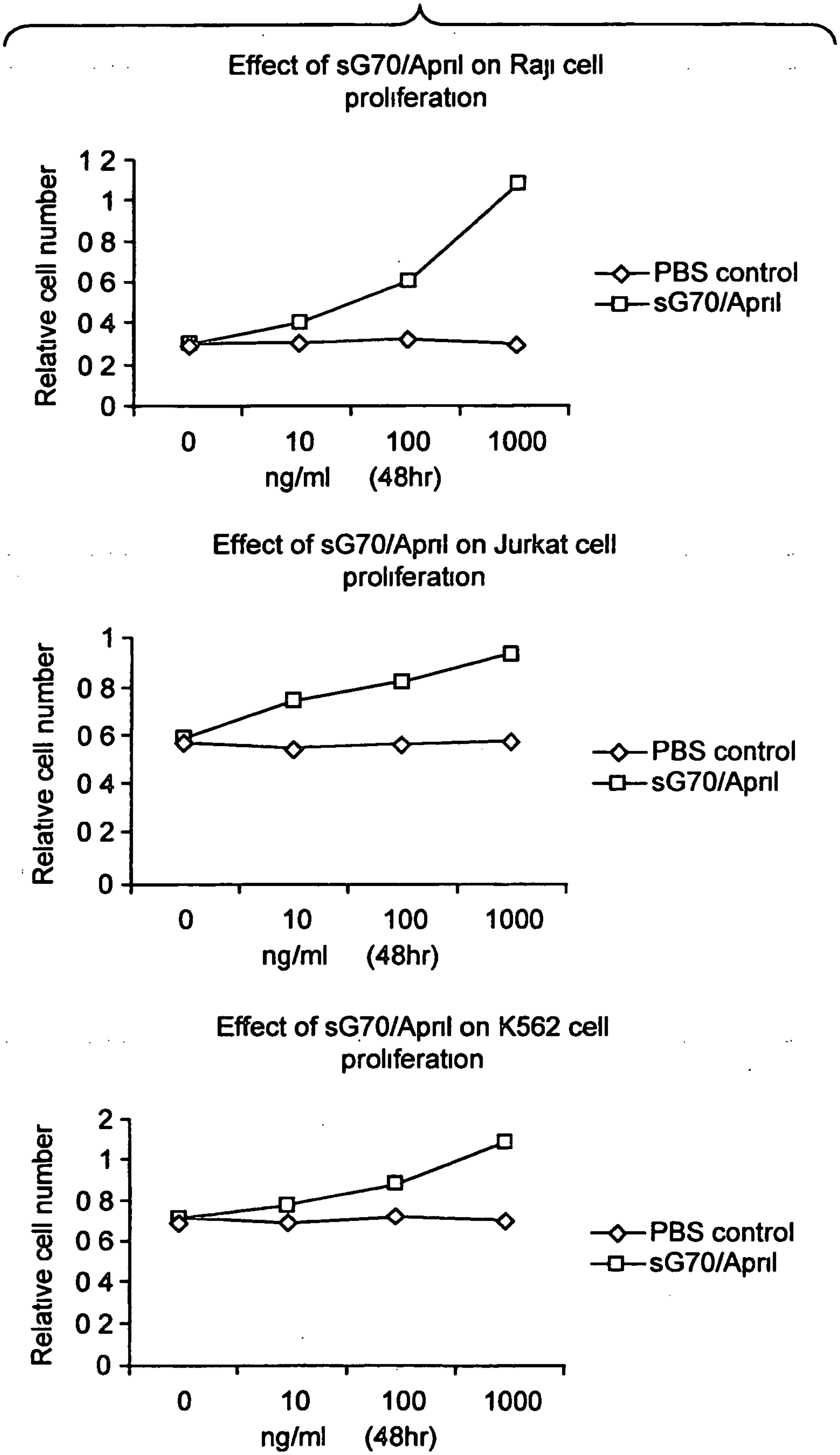

Effect of sG70/Apnl on Rajı cell prolıferatıon
Relative cell number
1 2
1
0 8
0 6
0 4
0 2
0
0
10
100
1000
ng/ml (48hr)
PBS control
sG70/Apnl
Effect of sG70/Apnl on Jurkat cell prolıferatıon
Relative cell number
1
0 8
0 6
0 4
0 2
0
0
10
100
1000
ng/ml (48hr)
PBS control
sG70/Apnl
Effect of sG70/Apnl on K562 cell prolıferatıon
Relative cell number
2
1
0 8
0 6
0 4
0 2
0
0
10
100
1000
ng/ml (48hr)
PBS control
sG70/Apnl

FIG. 4B

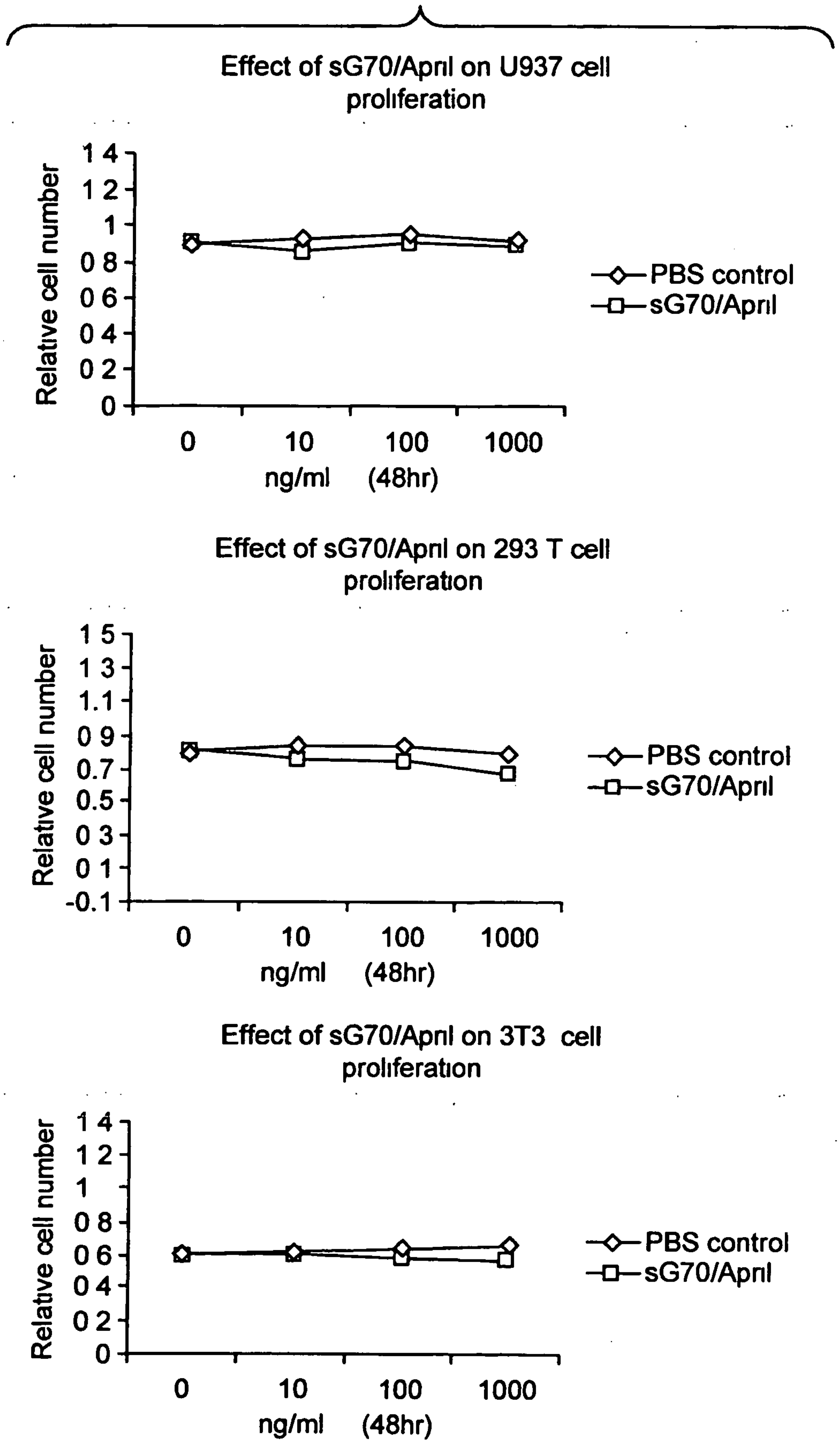

Effect of sG70/Apnl on U937 cell proliferation
Relative cell number
1 4
1 2
1
0 8
0 6
0 4
0 2
0
0
10
100
1000
ng/ml (48hr)
PBS control
sG70/Apnl
Effect of sG70/Apnl on 293 T cell proliferation
Relative cell number
1 5
1 3
1.1
0 9
0.7
0.5
0 3
0 1
-0.1
0
10
100
1000
ng/ml (48hr)
PBS control
sG70/Apnl
Effect of sG70/Apnl on 3T3 cell proliferation
Relative cell number
1 4
1 2
1
0 8
0 6
0 4
0 2
0
0
10
100
1000
ng/ml (48hr)
PBS control
sG70/Apnl

FIG. 5A

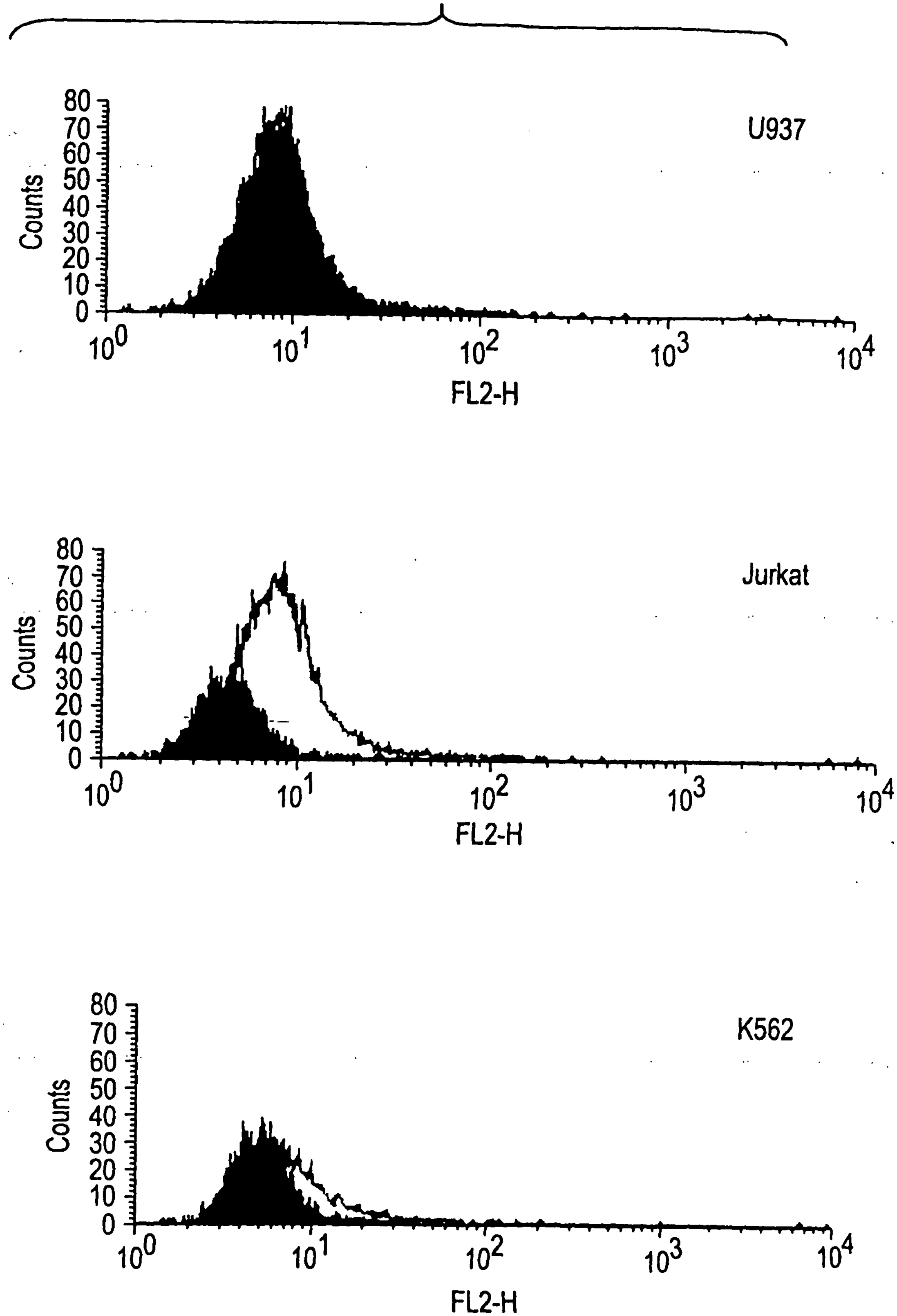


FIG. 5B-1

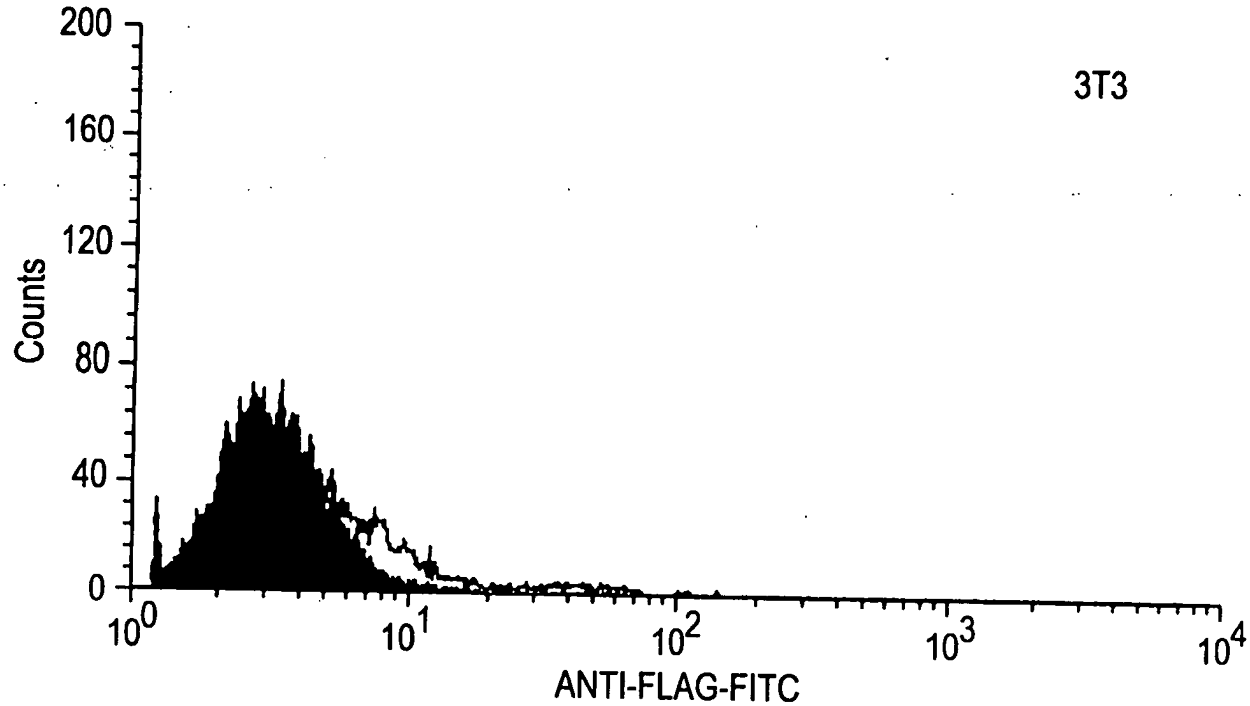


FIG. 5B-2

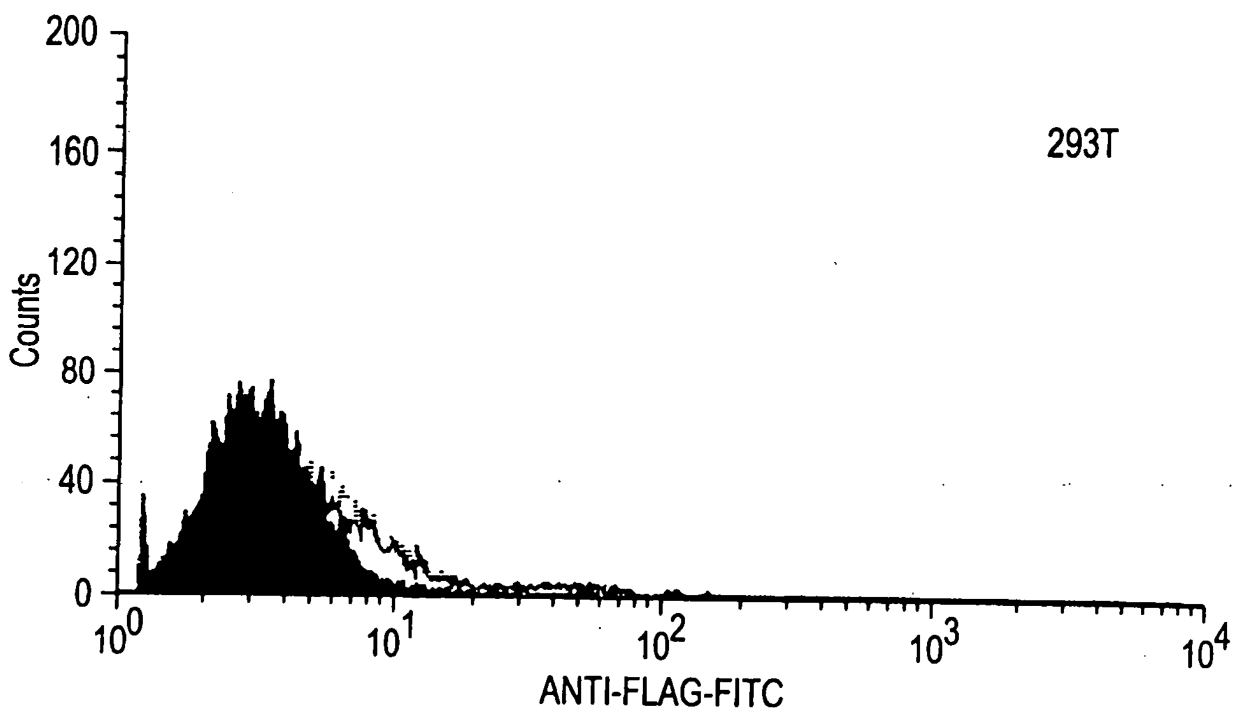


FIG. 5B-3

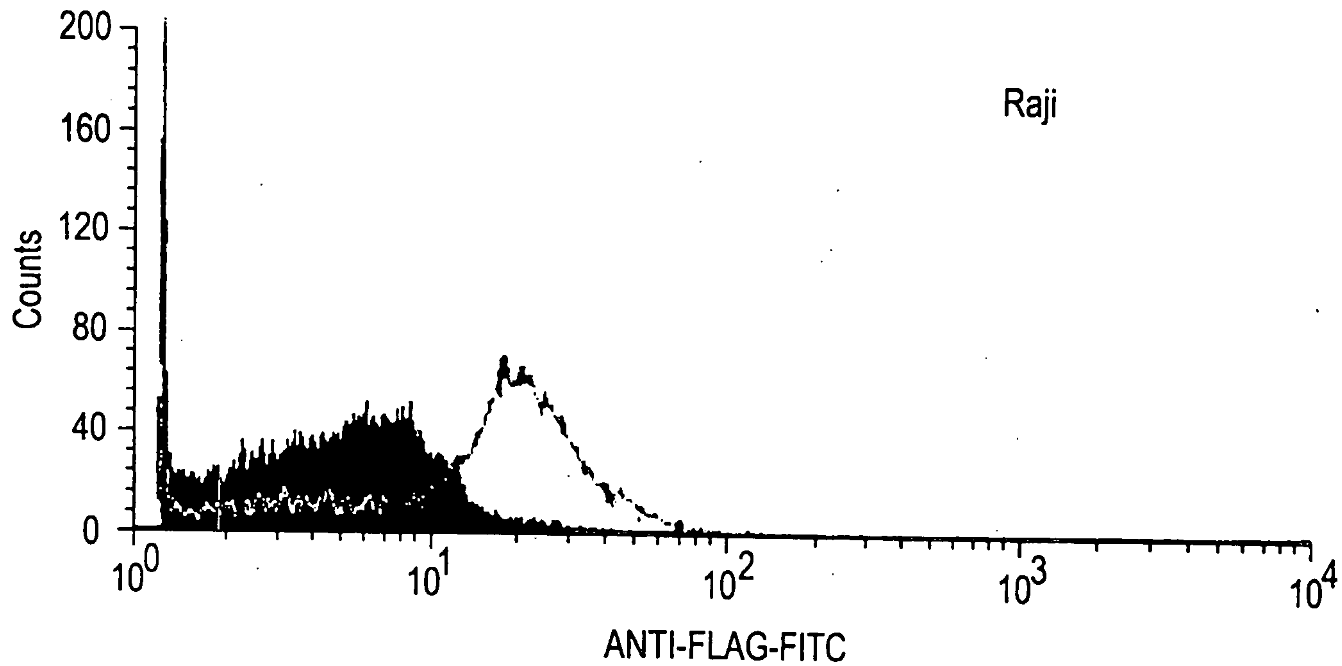
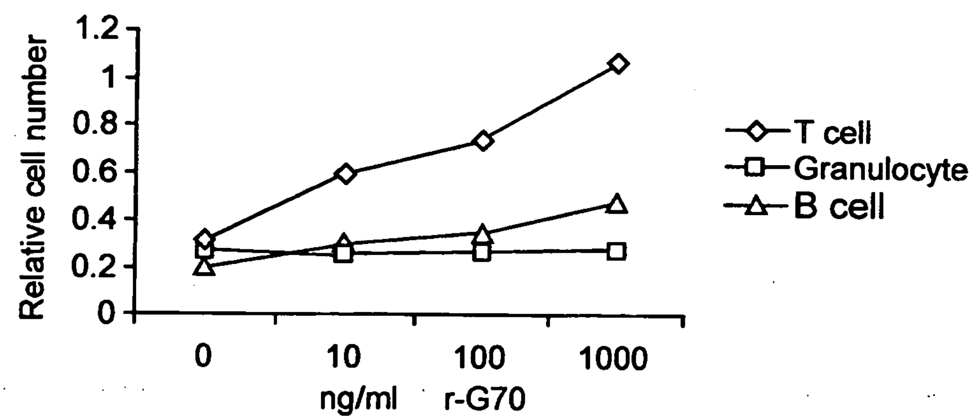

Raji
Counts
200
160
120
80
40
0
10^0
10^1
10^2
10^3
10^4
ANTI-FLAG-FITC

FIG. 6

The effect of r-G70/April on human peripheral blood B cell, T cell and Granucolyte



The effect of IL-2 and G70/April on human peripheral T cell proliferation

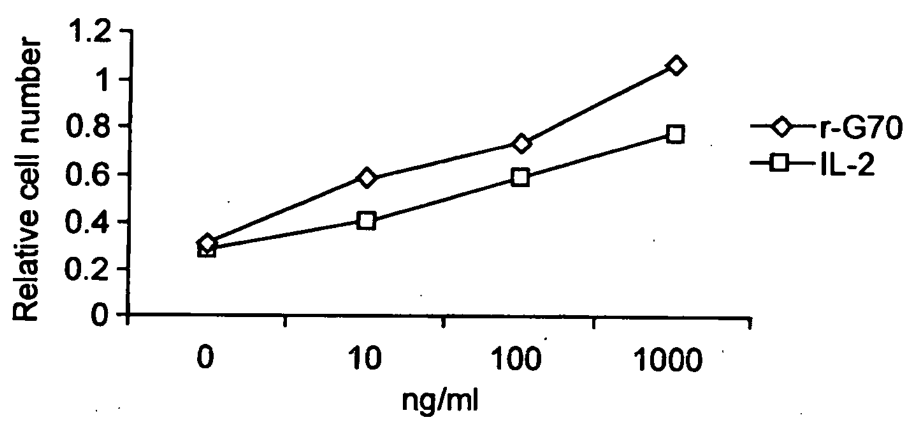
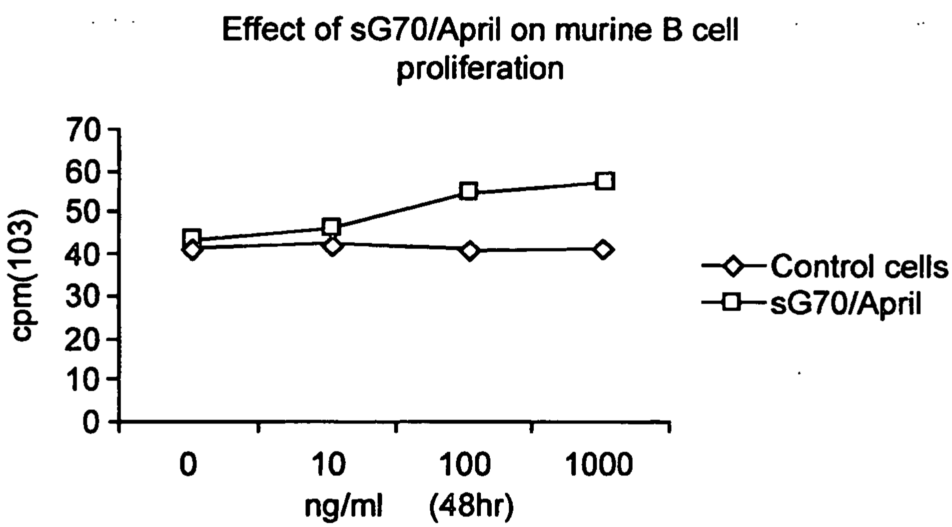


FIG. 7


Effect of sG70/April on murine B cell proliferation
70
60
50
40
30
20
10
0
cpm(103)
0
10
100
1000
ng/ml (48hr)
Control cells
sG70/April

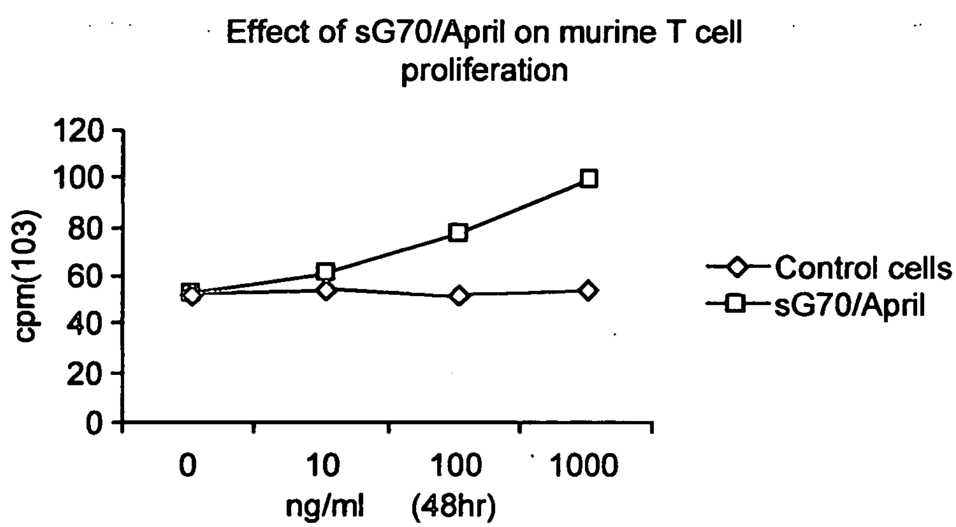
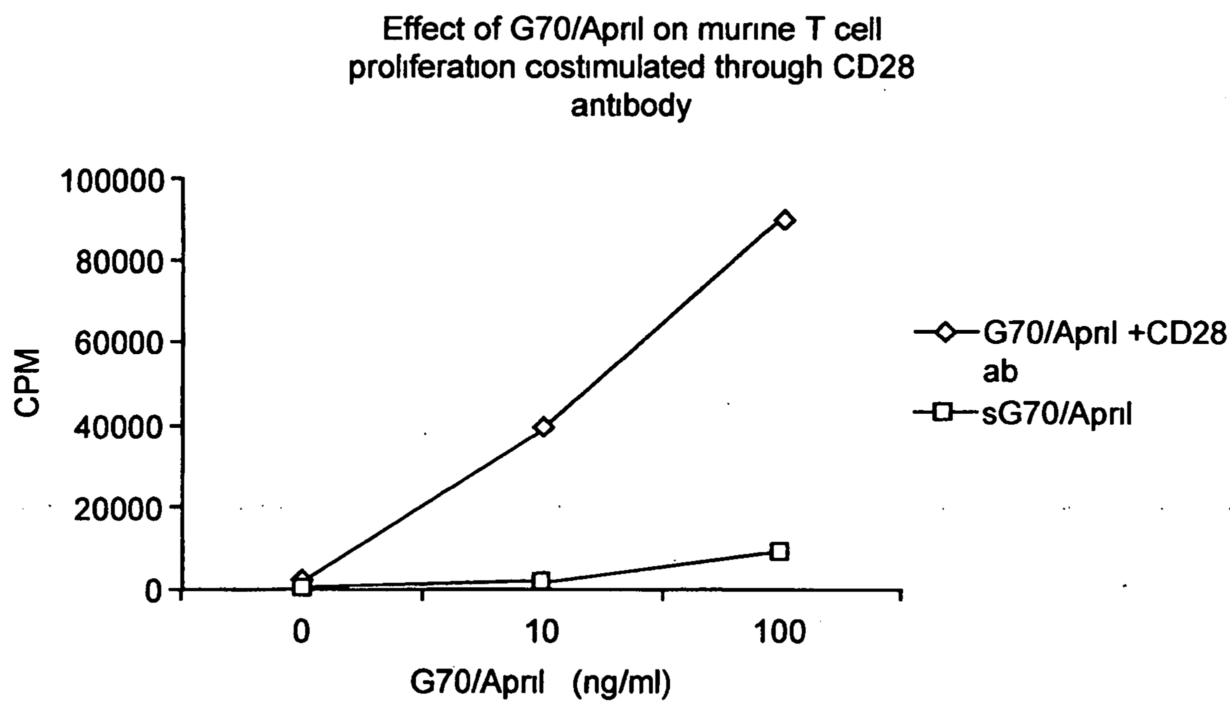
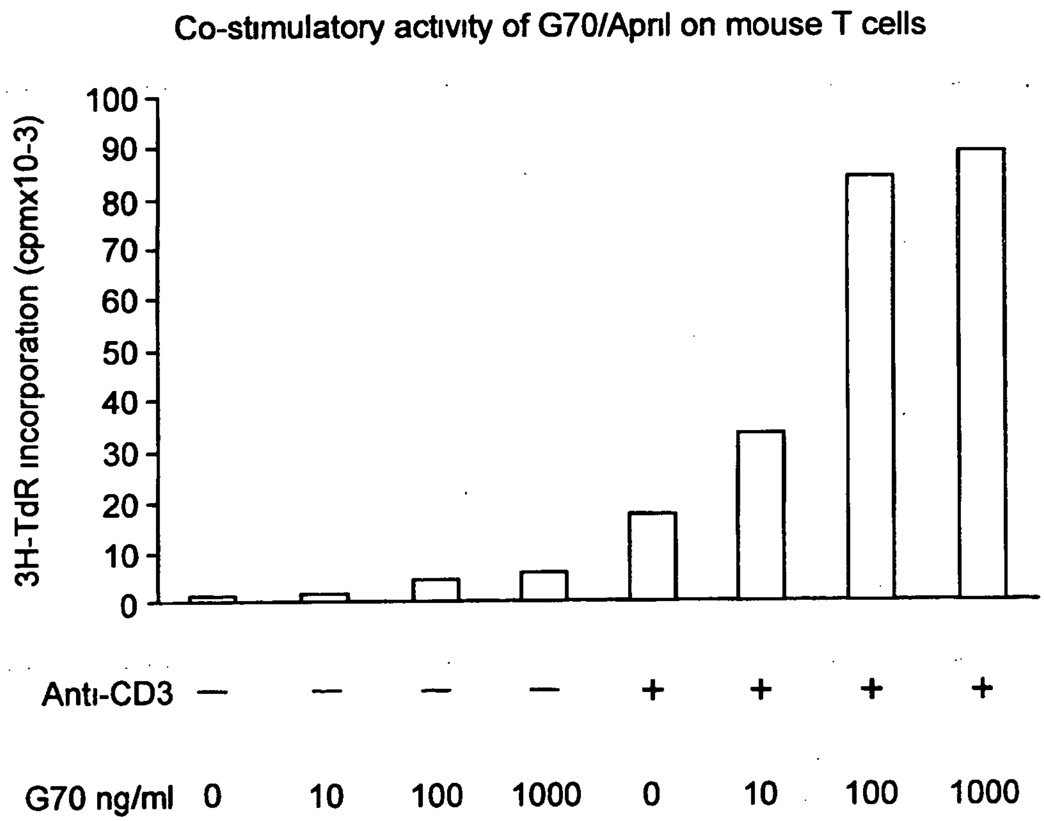

Effect of sG70/April on murine T cell proliferation
120
100
80
60
40
20
0
cpm(103)
0
10
100
1000
ng/ml (48hr)
Control cells
sG70/April

FIG. 8



Effect of G70/April on murine T cell proliferation costimulated through CD28 antibody
100000
80000
60000
40000
20000
0
CPM
0
10
100
G70/April (ng/ml)
G70/April +CD28 ab
sG70/April

FIG. 9



Co-stimulatory activity of G70/April on mouse T cells
3H-TdR incorporation (cpmx10-3)
100
90
80
70
60
50
40
30
20
10
0
Anti-CD3 — — — — + + + +
G70 ng/ml 0 10 100 1000 0 10 100 1000

FIG. 10A

Human BCMA

Human (SEQ ID NO: 5):

1 MAGQCSQNEY FDSLLHACIP CQLRCSSNTP PLTCQRYCNA SVTNSVKGTN

51 AILWTCLGLS LIISLAVFVL MFLLRKISSE PLKDEFKNTG SGLLGMANID

101 LEKSRTGDEI ILPRGLEYTV EECTCEDCIK SKPKVDSDHC FPLPAMEEGA

151 TILVTTKTND YCKSLPAALS ATEIEKSISA R

Human (SEQ ID NO: 5):

MAGQ**CSQ NEYFDSLLHA CIPCQLRCSS NTPPLTCQRY C**NASVTNSVK

GTNA <u>ILWTCL GLSLIISLAV FVLMF</u>LLRKI SSEPLKDEFK NTGSGLLGMA

NIDLEKSRTG DEIILPRGLE YTVEECTCED CIKSKPKVDS DHCFPLPAME

EGATILVTTK TNDYCKSLPA ALSATEIEKS ISAR

hBCMA's extracellular domain (SEQ ID NO: 6):

MAGQCSQ NEYFDSLLHA CIPCQLRCSS NTPPLTCQRY CNASVTNSVK

GTNA

hBCMA's cysteine-rich consensus region (SEQ ID NO: 7):

CSQ NEYFDSLLHA CIPCQLRCSS NTPPLTCQRY C

hBCMA's transmembrane region (SEQ ID NO: 8):

ILWTCL GLSLIISLAV FVLMF

FIG. 10B

huBCMA-Fc (SEQ ID NO 9)

MAGQCSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGTNAGGG
GGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK
FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG
QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS
LSLSPGK*

muBCMA-Fc (SEQ ID NO 10)

MAQQCFHSEYFDSLLHACKPCHLRCSNPPATCQPYCDPSVTSSVKGSYTGGGGG
DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN
WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLS
LSPGK*

FIG. 11

Alignment of human BCMA amino acid sequence and murine BCMA amino acid sequence

murine BCMA amino acid sequence Length 185 (SEQ ID NO 11)

```
  1  MAQQCFHSEY FDSLLHACKP CHLRCSNPPA TCQPYCDPSV TSSVKGTYTV

 51  LWIFLGLTLV LSLALFTISF LLRKMNPEAL KDEPQSPGQL DGSAQLDKAD

101  TELTRIRAGD DRIFPRSLEY TVEECTCEDC VKSKPKGDSD HFFPLPAMEE

151  GATILVTTKT GDYGKSSVPT ALQSVMGMEK PTHTR
```

alignment of human BCMA amino acid sequence and murine BCMA amino acid sequence

```
Query    4 MAGQCSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGTNAILWTCLGLS 63
           MA QC  +EYFDSLLHAC PC LRCS+  PP TCQ YC+ SVT+SVKGT  +LW  LGL+
Sbjct    1 MAQQCFHSEYFDSLLHACKPCHLRCSN--PPATCQPYCDPSVTSSVKGTYTVLWIFLGLT 58

Query   64 LIISLAVFVLMFLLRKISSEPLKDEFKNTG----SGLLGMANIDLEKSRTGDEIILPRGL 119
           L++SLA+F + FLLRK++ E LKDE ++ G    S  L  A+ +L + R GD+ I PR L
Sbjct   59 LVLSLALFTISFLLRKMNPEALKDEPQSPGQLDGSAQLDKADTELTRIRAGDDRIFPRSL 118

Query  120 EYTVEECTCEDCIKSKPKVDSDHCFPLPAMEEGATILVTTKTNDYCKS-LPAAL-SATEI 177
           EYTVEECTCEDC+KSKPK DSDH FPLPAMEEGATILVTTKT DY KS +P AL S   +
Sbjct  119 EYTVEECTCEDCVKSKPKGDSDHFFPLPAMEEGATILVTTKTGDYGKSSVPTALQSVMGM 178

Query  178 EKSISAR 184
           EK   R
Sbjct  179 EKPTHTR 185
```

FIG. 12A

Human TACI

huTACI (SEQ ID NO 14)

1 MSGLGRSRRG GRSRVDQEER FPQGLWTGVA MRSCPEEQYW DPLLGTCMSC

51 KTICNHQSQR TCAAFCRSLS CRKEQGKFYD HLLRDCISCA SICGQHPKQC

101 AYFCENKLRS PVNLPPELRR QRSGEVENNS DNSGRYQGLE HRGSEASPAL

151 PGLKLSADQV ALVYSTLGLC LCAVLCCFLV AVACFLKKRG DPCSCQPRSR

201 PRQSPAKSSQ DHAMEAGSPV STSPEPVETC SFCFPECRAP TQESAVTPGT

251 PDPTCAGRWG CHTRTTVLQP CPHIPDSGLG IVCVPAQEGG PGA

MSGLGRSRRGGRSRVDQEERFPQGLWTGVAMRSCPEEQYWDPLLGTCMSC
KTICNHQSQRTCAAFCRSLSCRKEQGKFYDHLLRDCISCASICGQHPKQC
AYFCENKLRSPVNLPPELRRQRSGEVENNSDNSGRYQGLEHRGSEASPAL
PGLKLSADQVALVYST<u>LGLCLCAVLCCFLVAVACFL</u>KKRGDPCSCQPRSR
PRQSPAKSSQDHAMEAGSPVSTSPEPVETCSFCFPECRAPTQESAVTPGT
PDPTCAGRWGCHTRTTVLQPCPHIPDSGLGIVCVPAQEGGPGA

huTACI's extracellular domain (SEQ ID NO 15)

1 MSGLGRSRRG GRSRVDQEER FPQGLWTGVA MRSCPEEQYW DPLLGTCMSC

51 KTICNHQSQR TCAAFCRSLS CRKEQGKFYD HLLRDCISCA SICGQHPKQC

101 AYFCENKLRS PVNLPPELRR QRSGEVENNS DNSGRYQGLE HRGSEASPAL

151 PGLKLSADQV ALVYST

FIG. 12B

huTACI's cysteine-rich consensus region (SEQ ID NO: 16):
CPEEQYWDPLLGTCMSCKTICNHQSQRTCAAFC and
CRKEQGKFYDHLLRDCISCASICGQHPKQCAYFC

transmembrane region (SEQ ID NO: 17):
LGLCLCAVLCCFLVAVACFL

hTACI-Fc (SEQ ID NO: 18):

1 MSGLGRSRRG GRSRVDQEER FPQGLWTGVA MRSCPEEQYW DPLLGTCMSC

51 KTICNHQSQR TCAAFCRSLS CRKEQGKFYD HLLRDCISCA SICGQHPKQC

101 AYFCENKLRS PVNLPPELRR QRSGEVENNS DNSGRYQGLE HRGSEASPAL

151 PGLKLSADQV ALVYSGGGGG DKTHTCPPCP APELLGGPSV FLFPPKPKDT

201 LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY

251 RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT

301 LPPSRDELTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTPPVLDS

351 DGSFFLYSKL TVDKSRWQQG NVFSCSVMHE ALHNHYTQKS LSLSPGK*

FIG. 13

Alignment of cysteine rich extracellular regions of human TACI and human BCMA

```
34 CPEEQYWDPLLGTCMSCKTICNHQS QRTCAAFCRSLSCRKEQGKFYDHL 82
   |    | | ||  |  |   |       ||   |         |
 8 CSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGT  NAI 55

       83 LRDCISCASI 92
          |  |     |
       56 LWTCLGLSLI 65
```

FIG. 14A

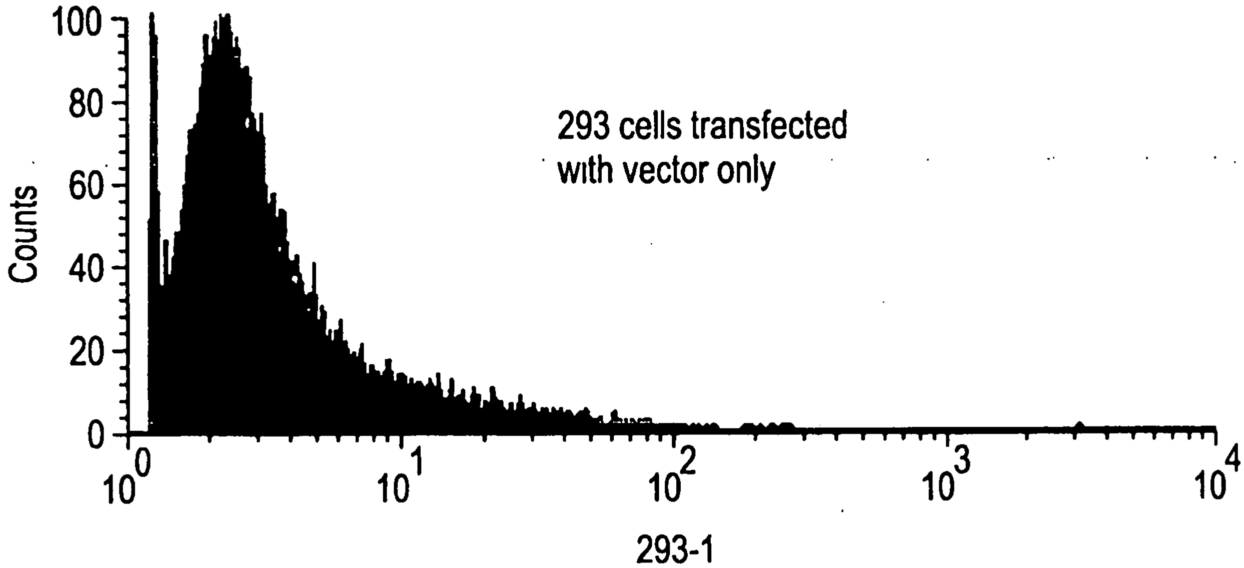


FIG. 14B

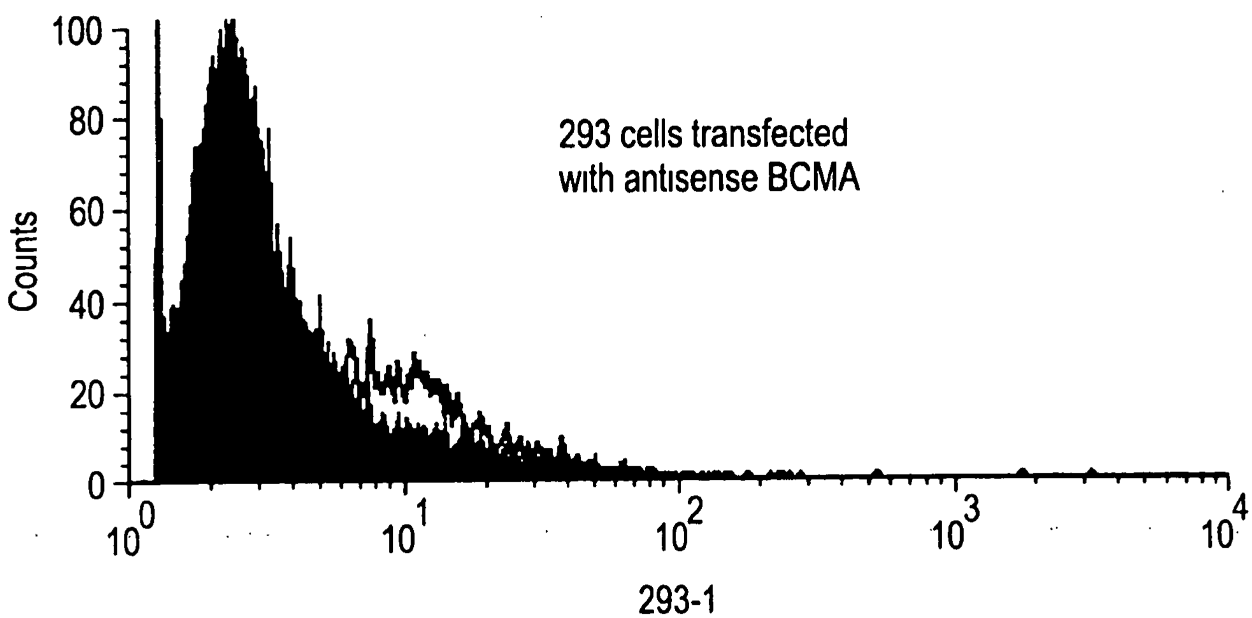
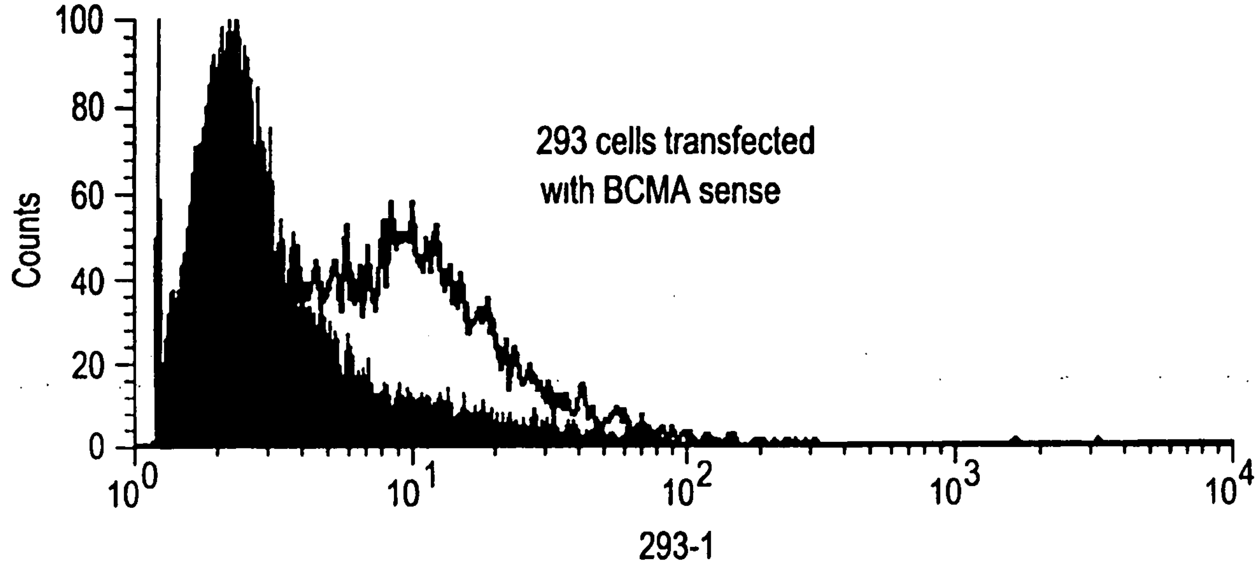


FIG. 14C



100
80
60
40
20
0
Counts
293 cells transfected
with BCMA sense
10^0
10^1
10^2
10^3
10^4
293-1

FIG. 15A

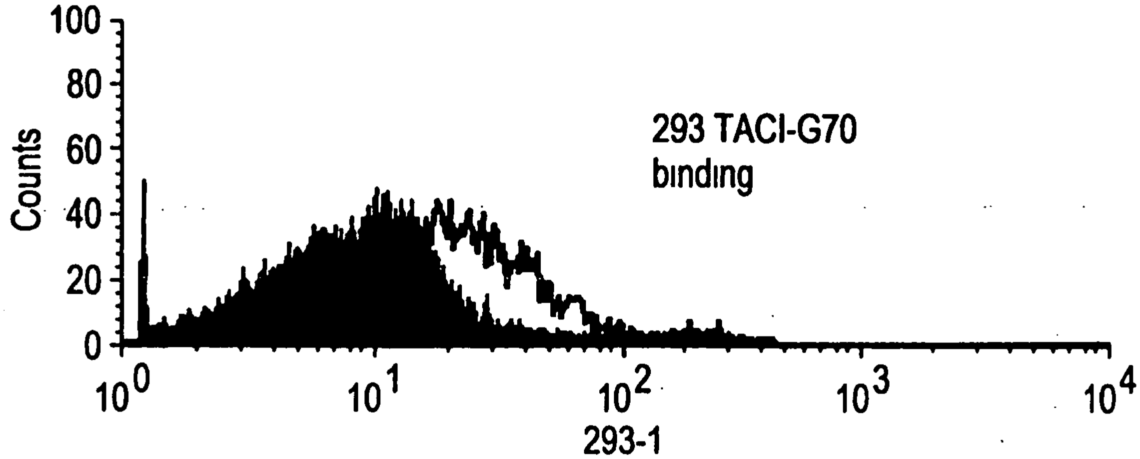


FIG. 15B

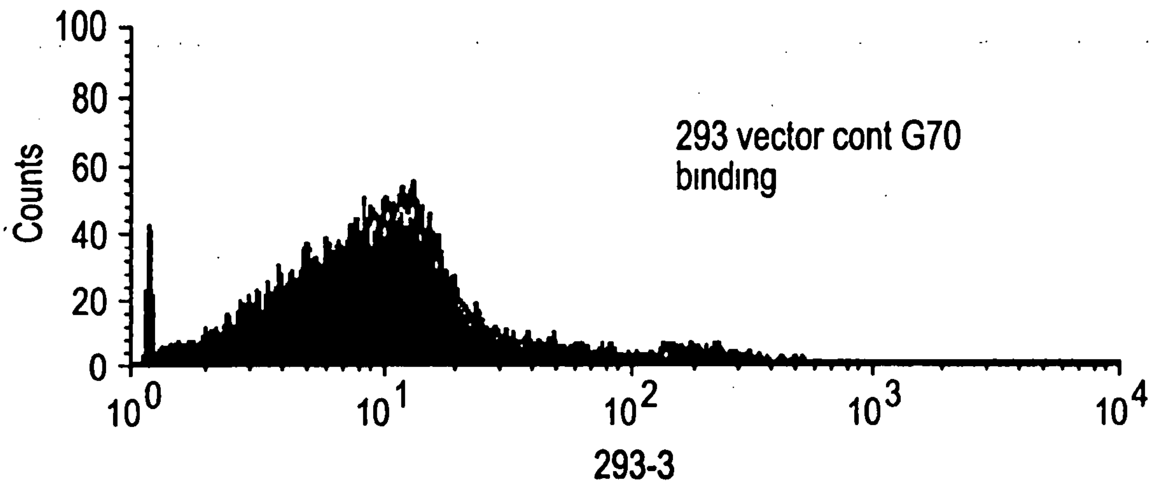


FIG. 16A

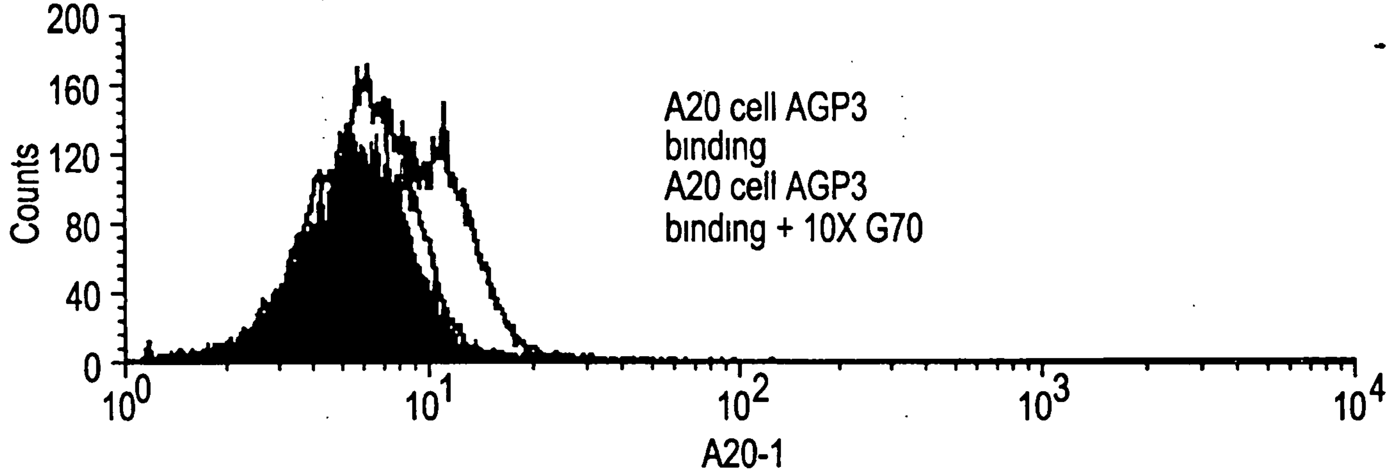


FIG. 16B

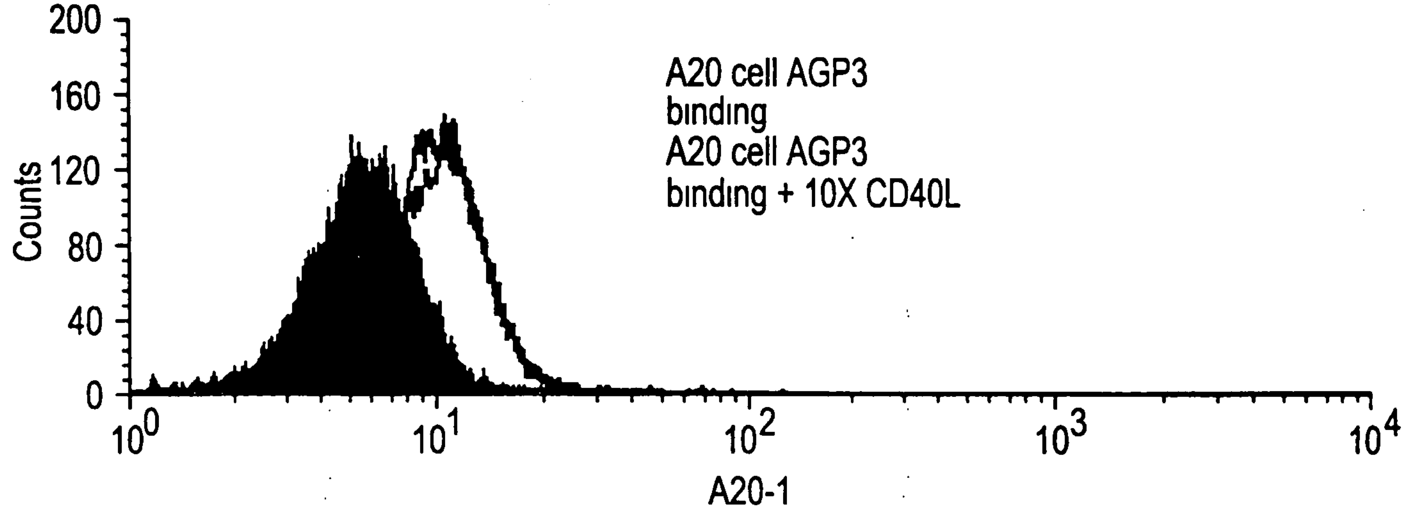


FIG. 16C

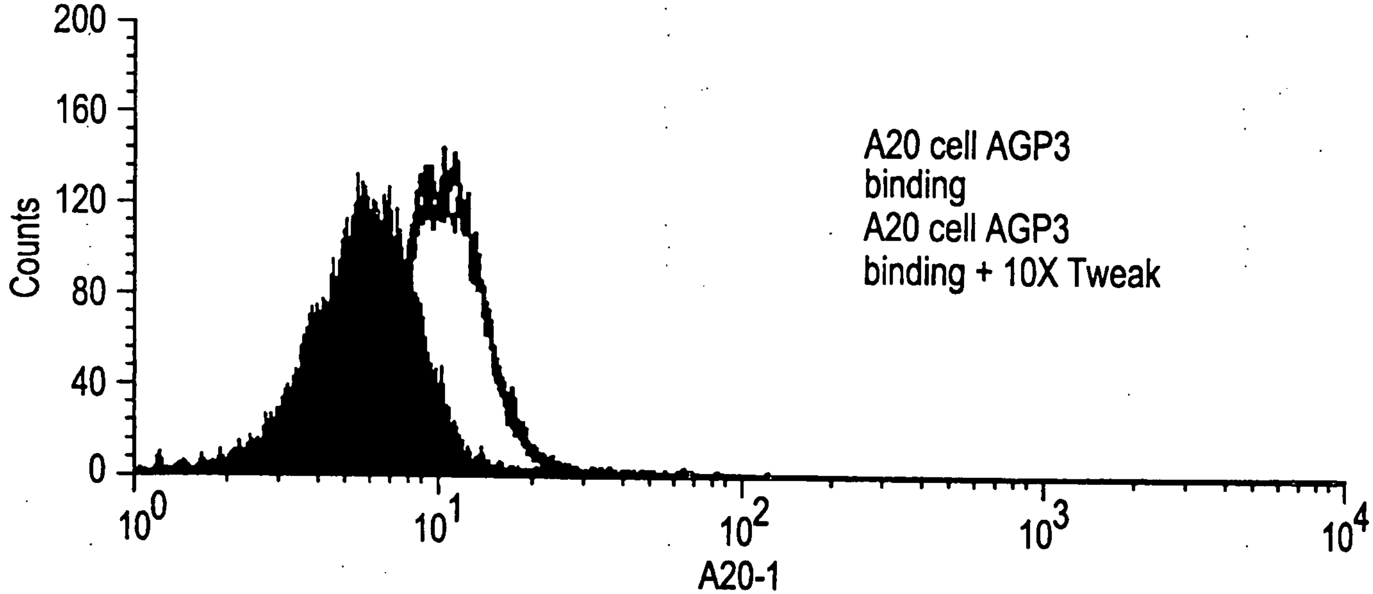


FIG. 16D

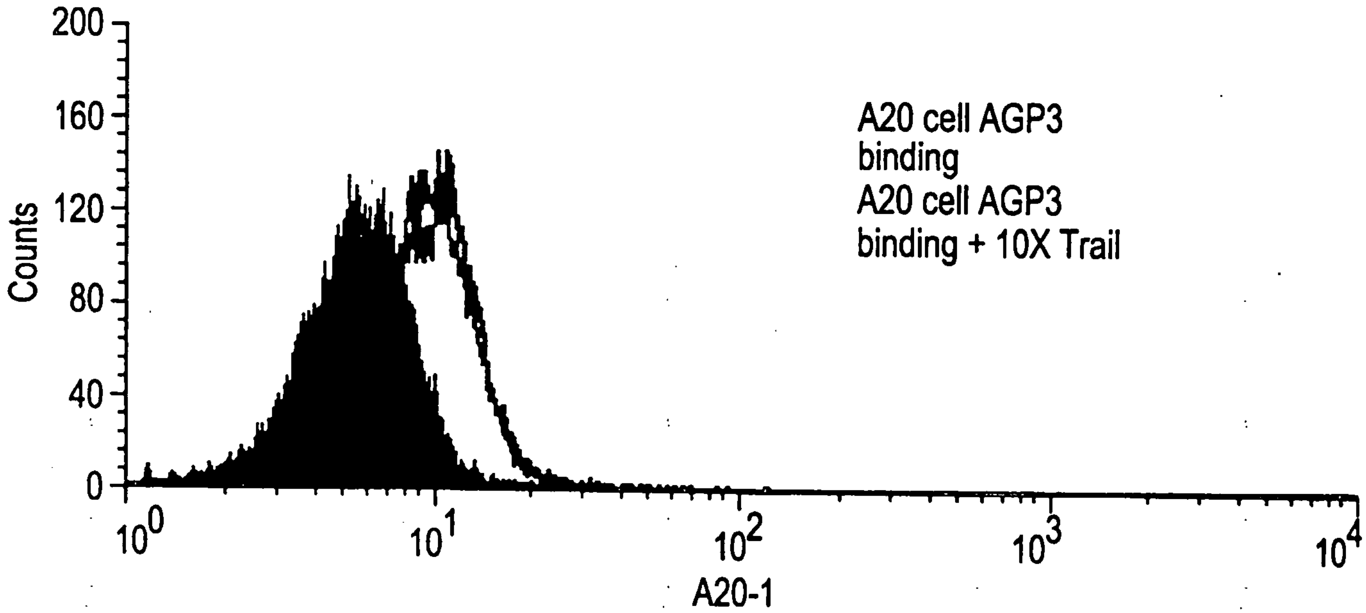


FIG. 17A

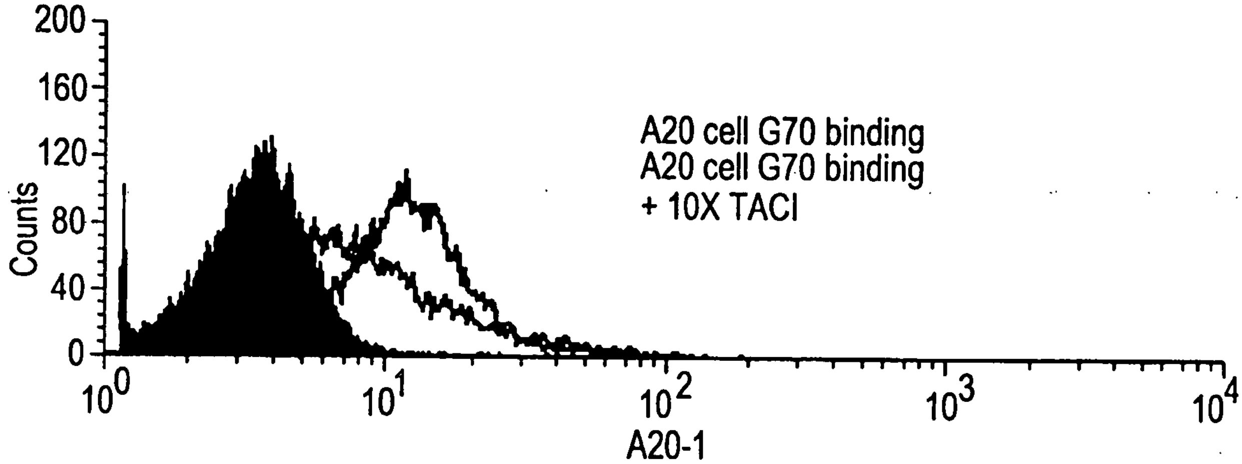


FIG. 17B

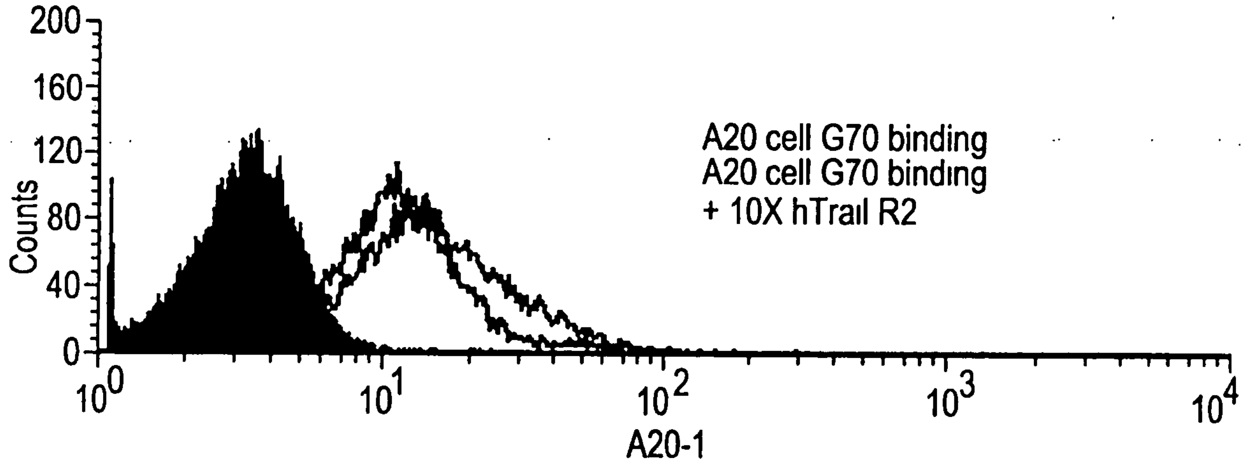


FIG. 17C

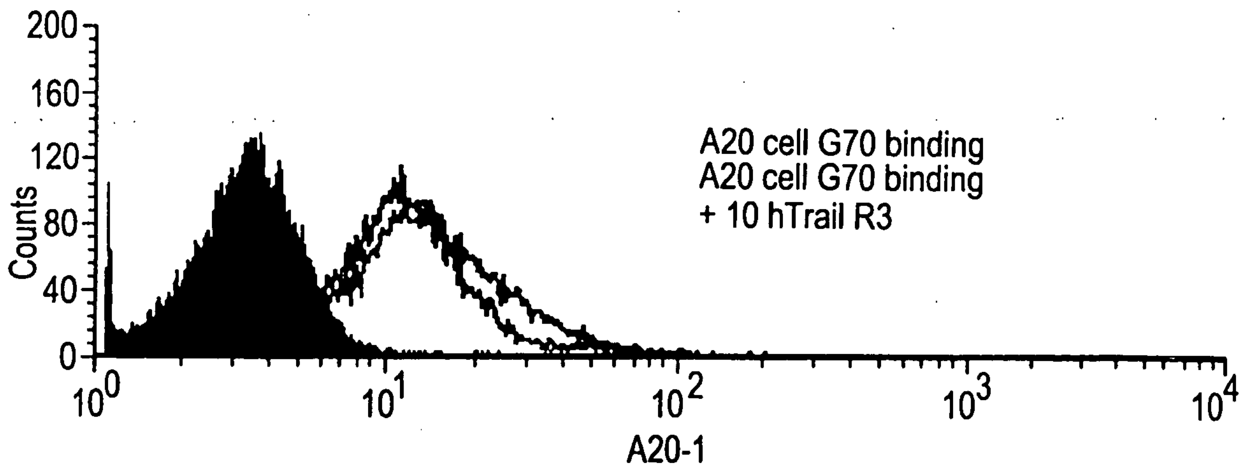
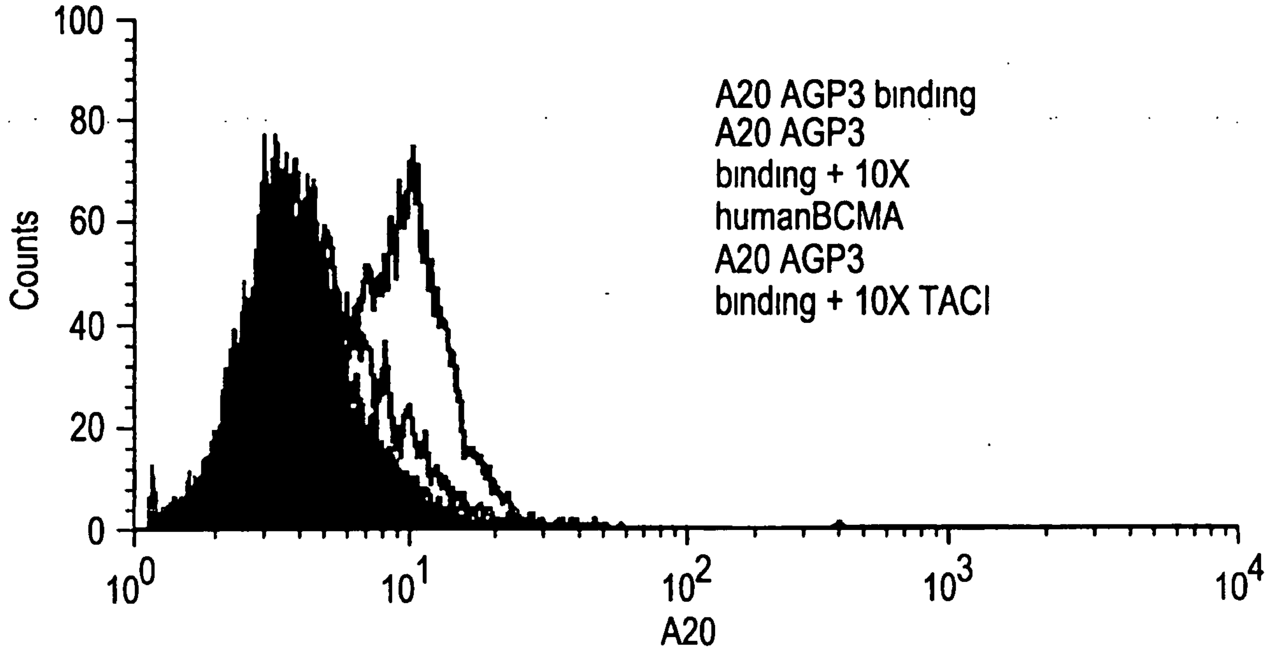


FIG. 18



A20 AGP3 binding
A20 AGP3 binding + 10X humanBCMA
A20 AGP3 binding + 10X TACI
Counts
100
80
60
40
20
0
10^0
10^1
10^2
10^3
10^4
A20

FIG. 19A

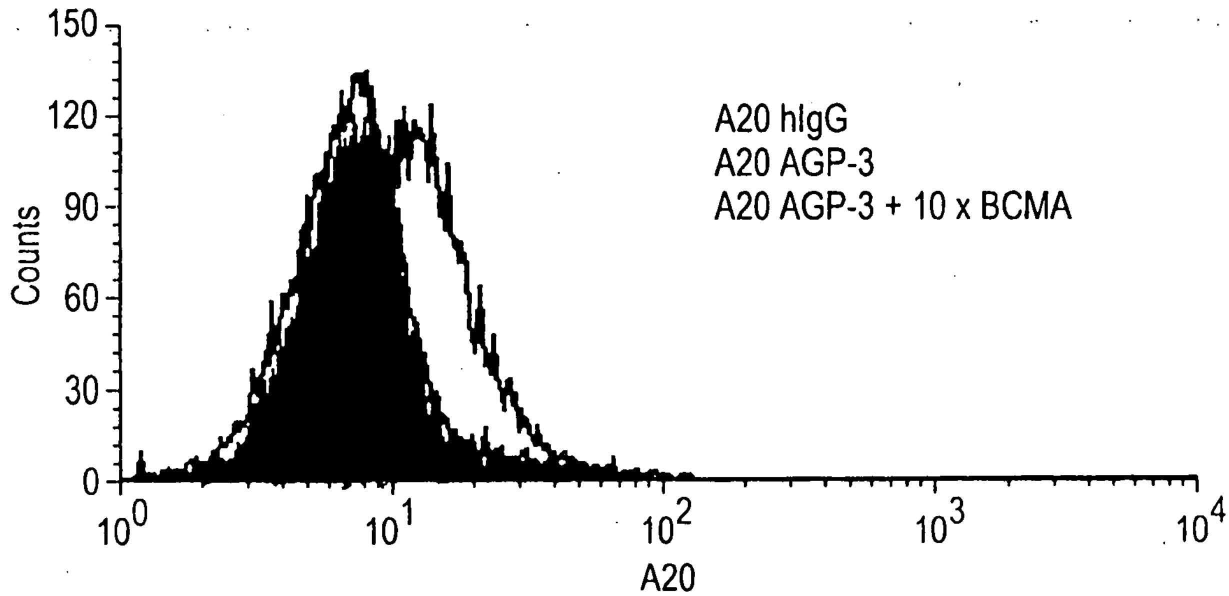


FIG. 19B

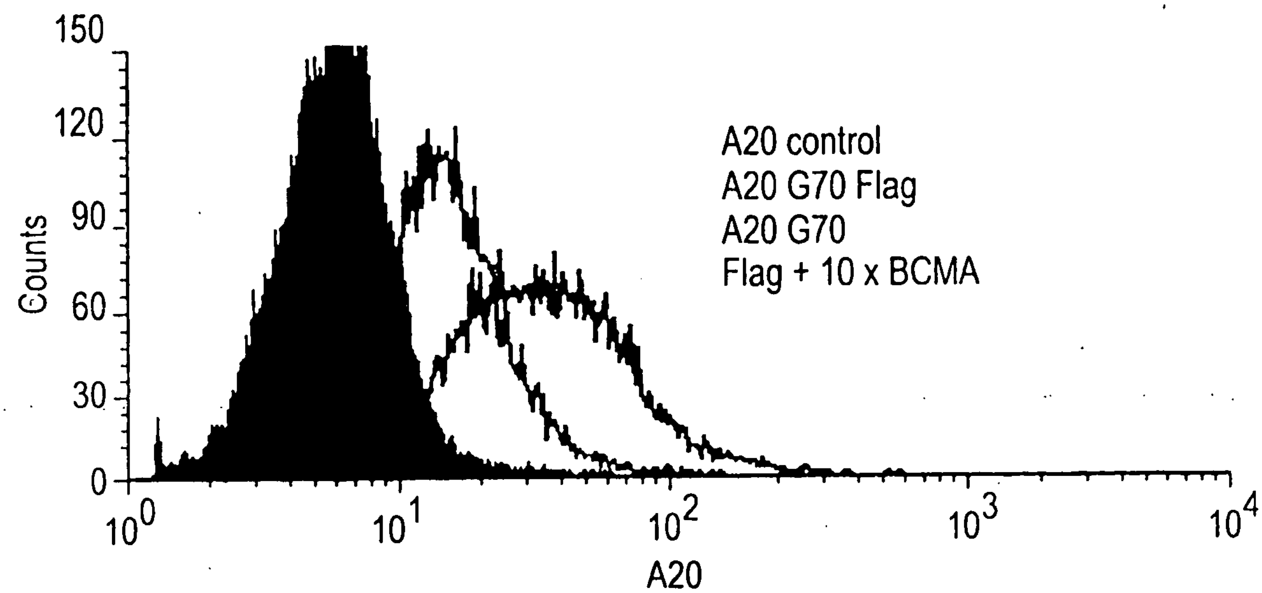


FIG. 20A

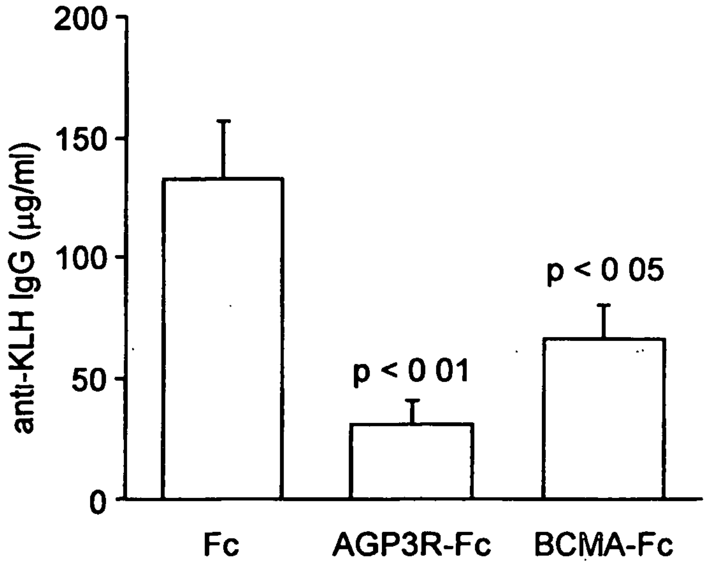


FIG. 20B

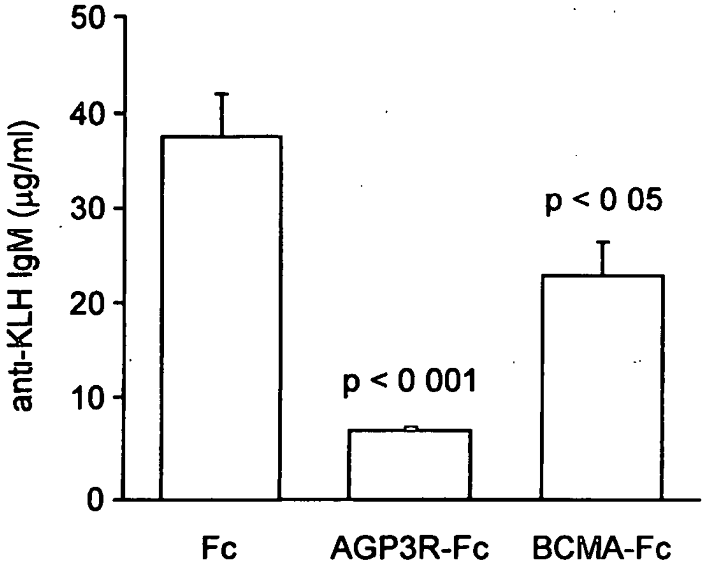


FIG. 20C

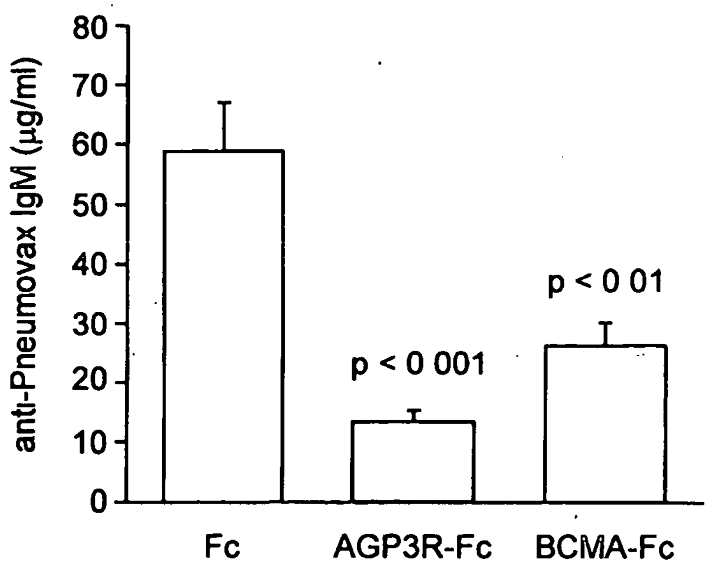


FIG. 21

Fc-humanAPRIL

Fc-humanAPRIL protein sequence including the signal sequence, Fc domain, linker (XhoI site) and APRIL

```
  1  MEWSWVFLFF LSVTTGVHSD KTHTCPPCPA PELLGGPSVF
     LFPPKPKDTL
 51  MISRTPEVTC VVVDVSHEDP EVKFNWYVDG VEVHNAKTKP
     REEQYNSTYR
101  VVSVLTVLHQ DWLNGKEYKC KVSNKALPAP IEKTISKAKG
     QPREPQVYTL
151  PPSRDELTKN QVSLTCLVKG FYPSDIAVEW ESNGQPENNY
     KTTPPVLDSD
201  GSFFLYSKLT VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL
     SLSPGK  SRAV
251  LTQKQKKQHS VLHLVPINAT SKDDSDVTEV MWQPALRRGR
     GLQAQGYGVR
301  IQDAGVYLLY SQVLFQDVTF TMGQVVSREG QGRQETLFRC
     IRSMPSHPDR
351  AYNSCYSAGV FHLHQGDILS VIIPRARAKL NLSPHGTFLG
     FVKL*
```

FIG. 22

Fc-HumanAPRIL and soluble human AGP3 stimulate proliferation of primary B cells

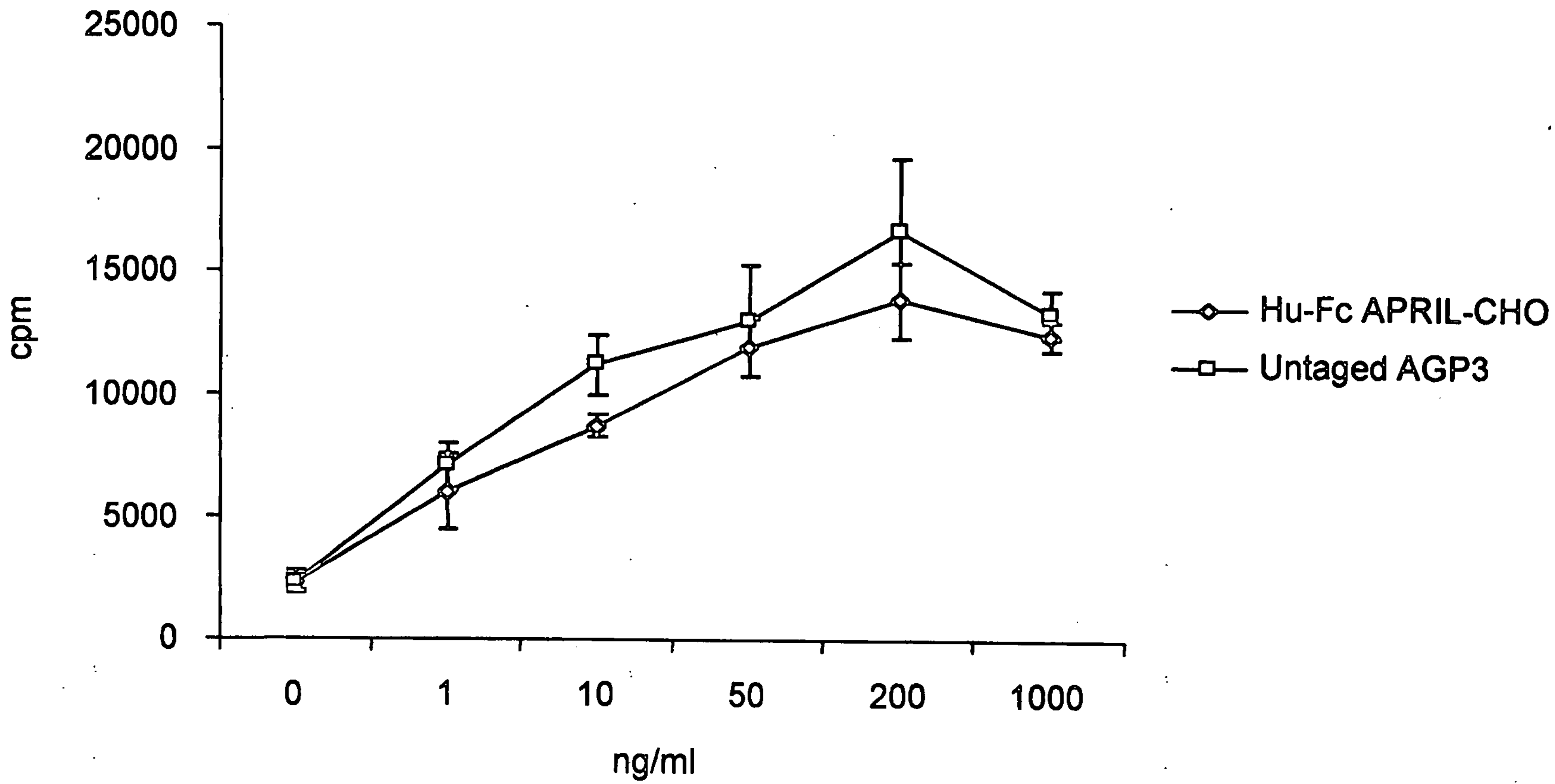


FIG. 23

hBCMA-Fc and wt hTACI-Fc inhibits Flag-mAPRIL mediated mouse B cell proliferation

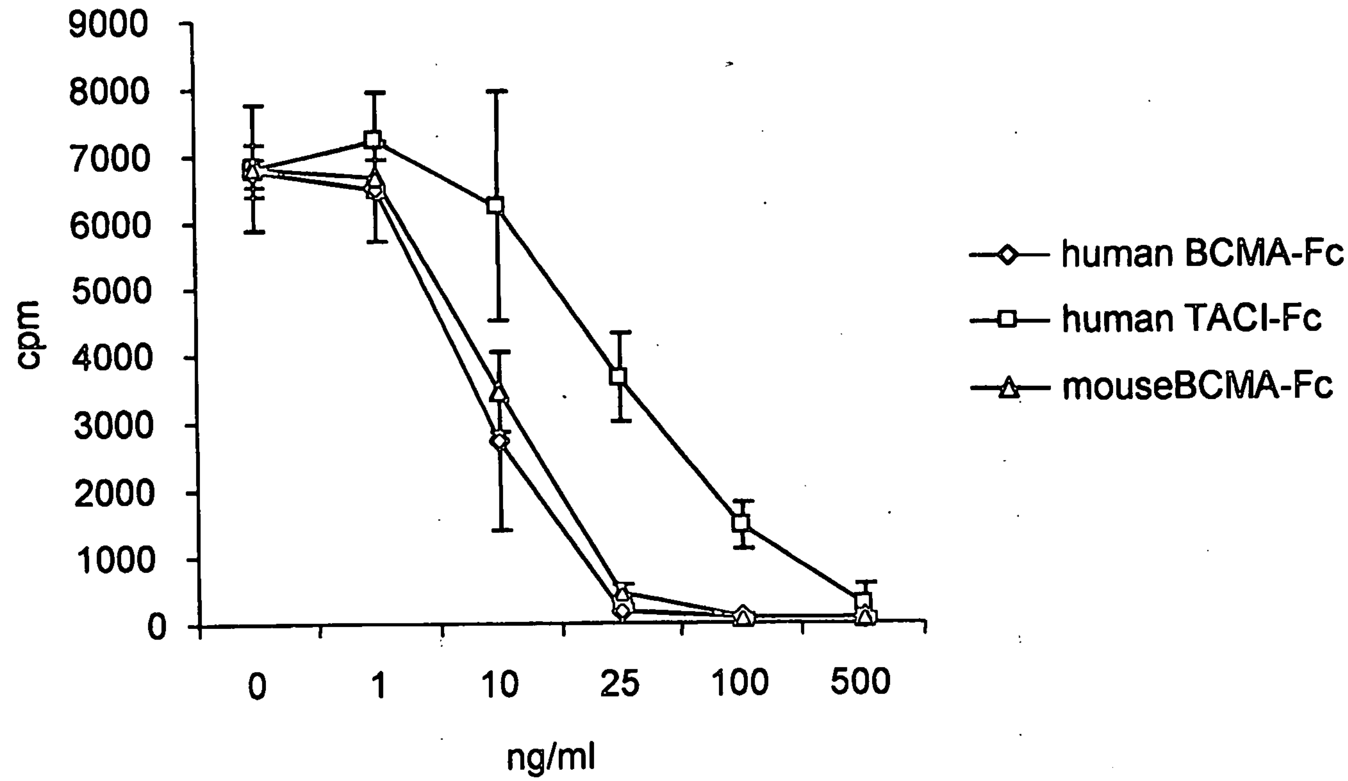


FIG. 24

hBCMA-Fc reduces PB B cell level *in vivo*

15 mg/kg ip on day 0, 3, and 6

BLOOD	WBC 10e6/ml	#Lym 10e6/ml	CD3+ #	CD3-B220+ #
BCMA-Fc	5 30	3 81	2 3	1 3
SD	0 39	0 43	0 32	0 27
t test	0 03318	0 01570	0 24737	0 00506
Fc	8 02	6 43	2 7	3 2
SD	1 27	1 52	0 6	0 6
Saline	6 90	5 55	2 1	2 9
SD	2 04	1 79	0 5	1 2

FIG. 25

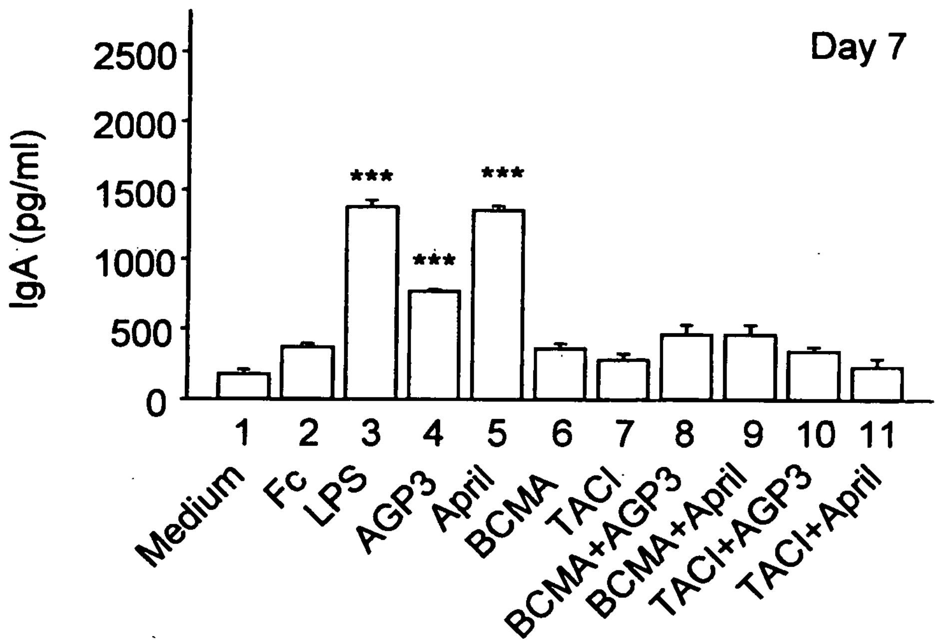
hBCMA-Fc reduces spleen B cell levels *in vivo*

15 mg/kg ip on day 0, 3, and 6

Spleen	WBC 10e6/ml	Lym (%)	spleen lym# 10ml(x10e6)	CD3-B220+ (%)	CD3-B220+ #
BCMA-Fc	9 12	97 9	89 3	45 5	41 8
SD	0 92	0 51	9 32	1 29	4 92
t test	0 02778	0 89118	0 02668	0 00234	0 02088
Fc	11 49	97 9	112 5	50 6	57 1
SD	1 62	0 38	15 65	1 95	9 67
Saline	11 48	98 5	113 1	53 7	48 5
SD	1 71	0 1	16 9	6 7	29 15

FIG. 26

Flag-mAPRIL and hAGP3 mediated IgA production inhibited by hBCMA-Fc and hTACI-Fc *in vitro*



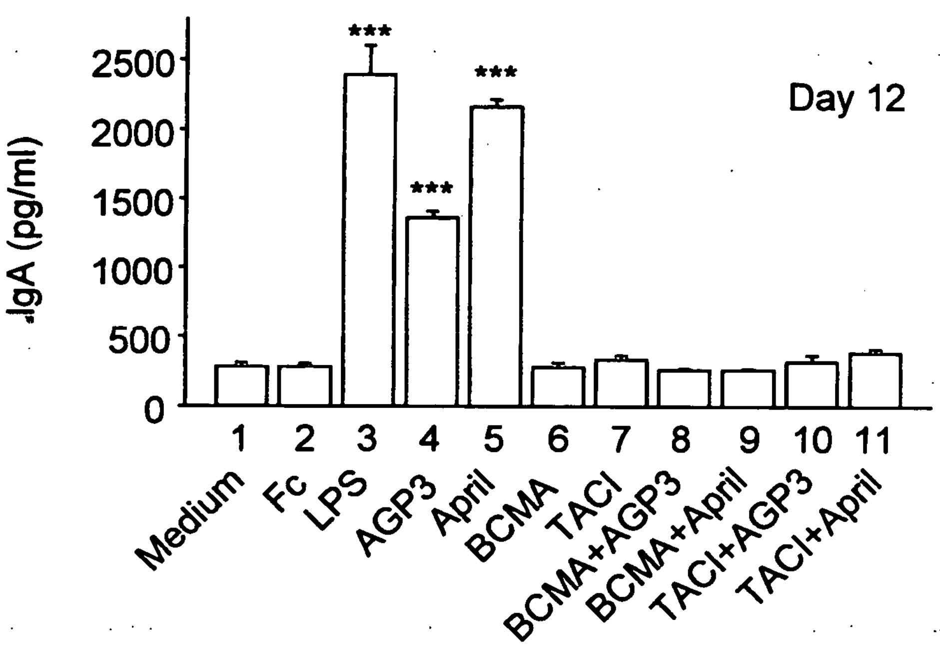


FIG. 27

Flag-mAPRIL and hAGP3 Mediated IgG Production Inhibited by BCMA-Fc and TACI-Fc *in Vitro*

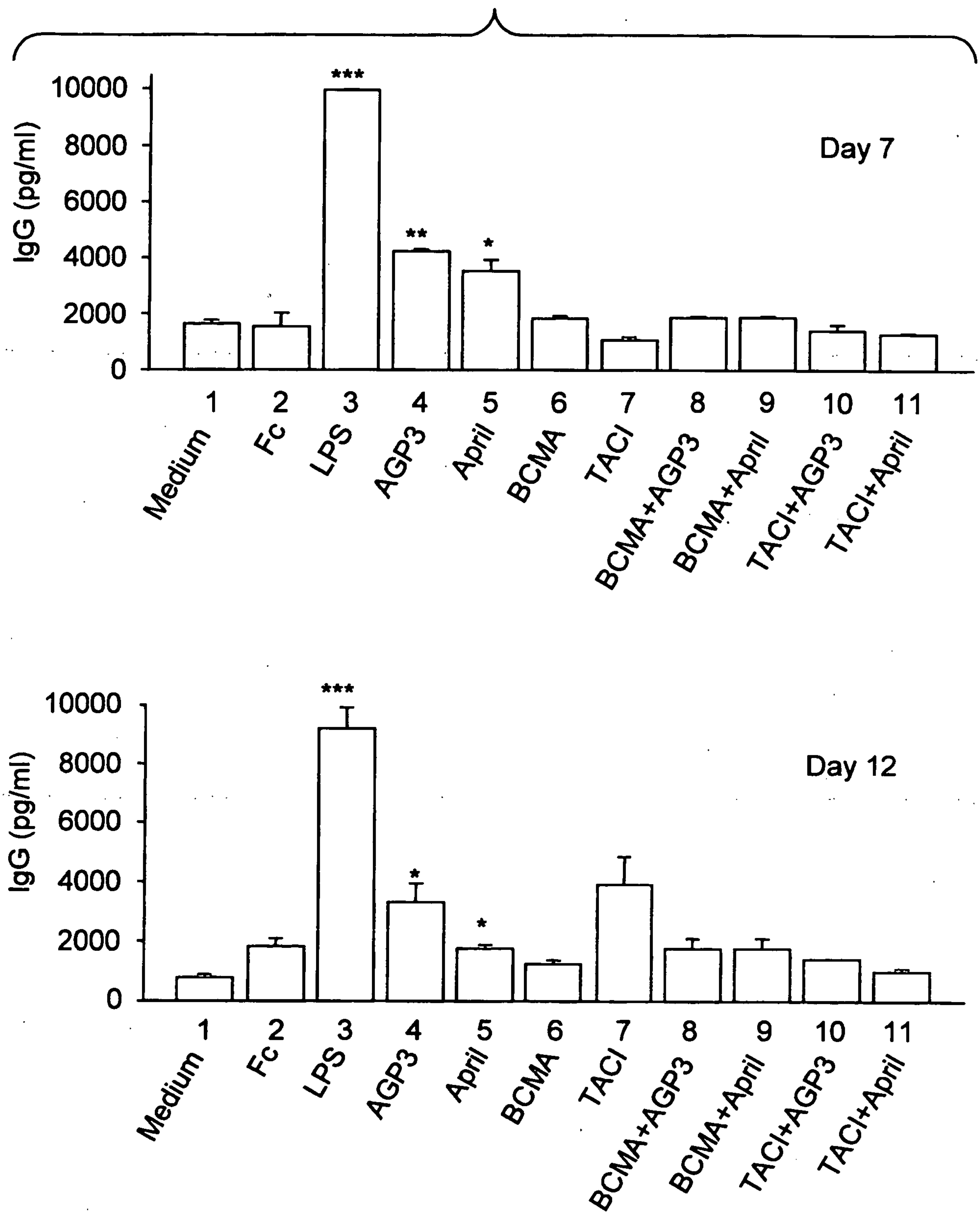


FIG. 28

Significantly reduces total IgE and IgA in normal mice treated with mBCMA-Fc and trun hTACI-Fc *5 mg/kg ip day 0, 3, and 6*

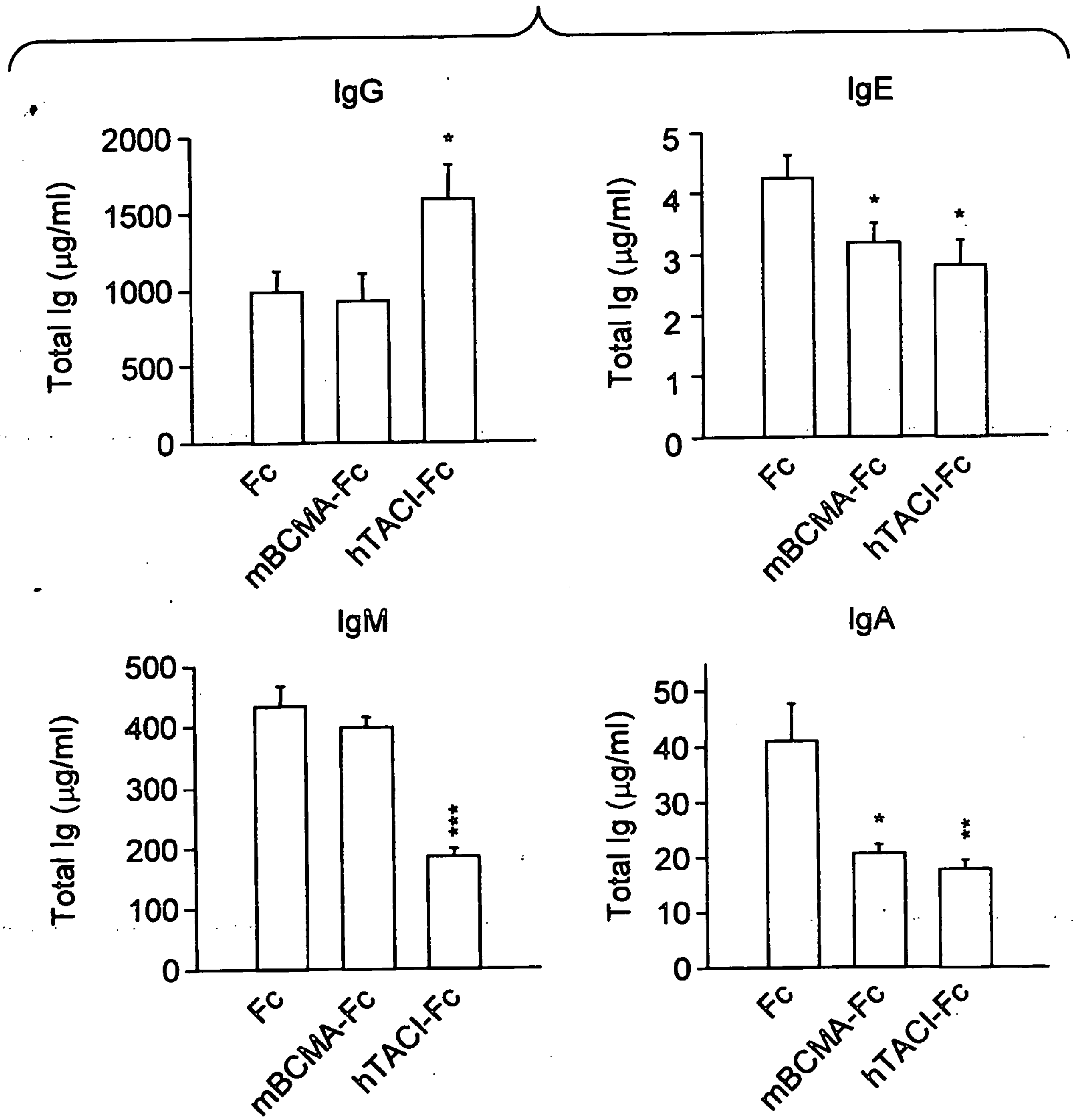


FIG. 29

BCMA-Fc and truncated TACI-Fc at daily doses of 0 5 mg/kg inhibits humoral immunity *in vivo*

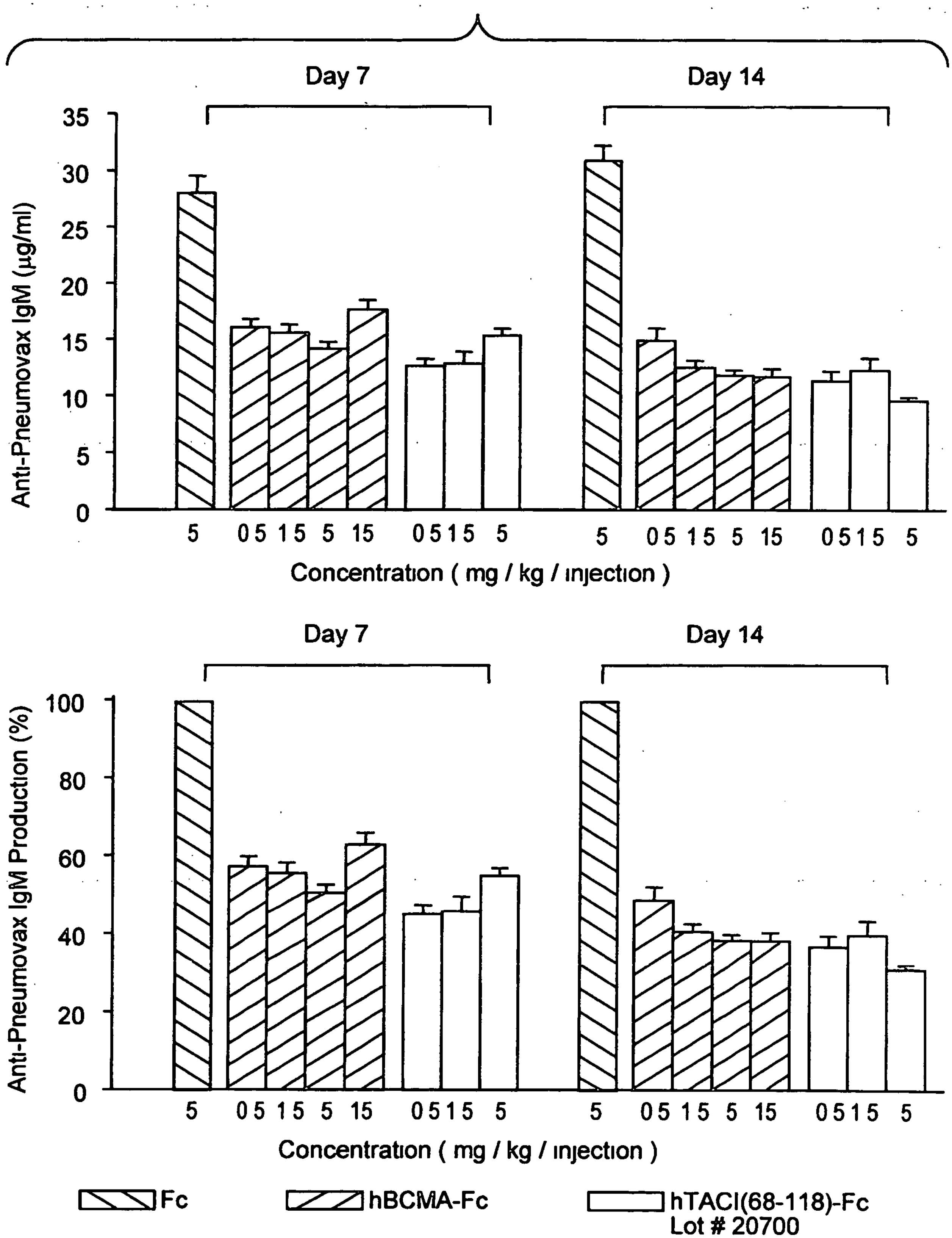
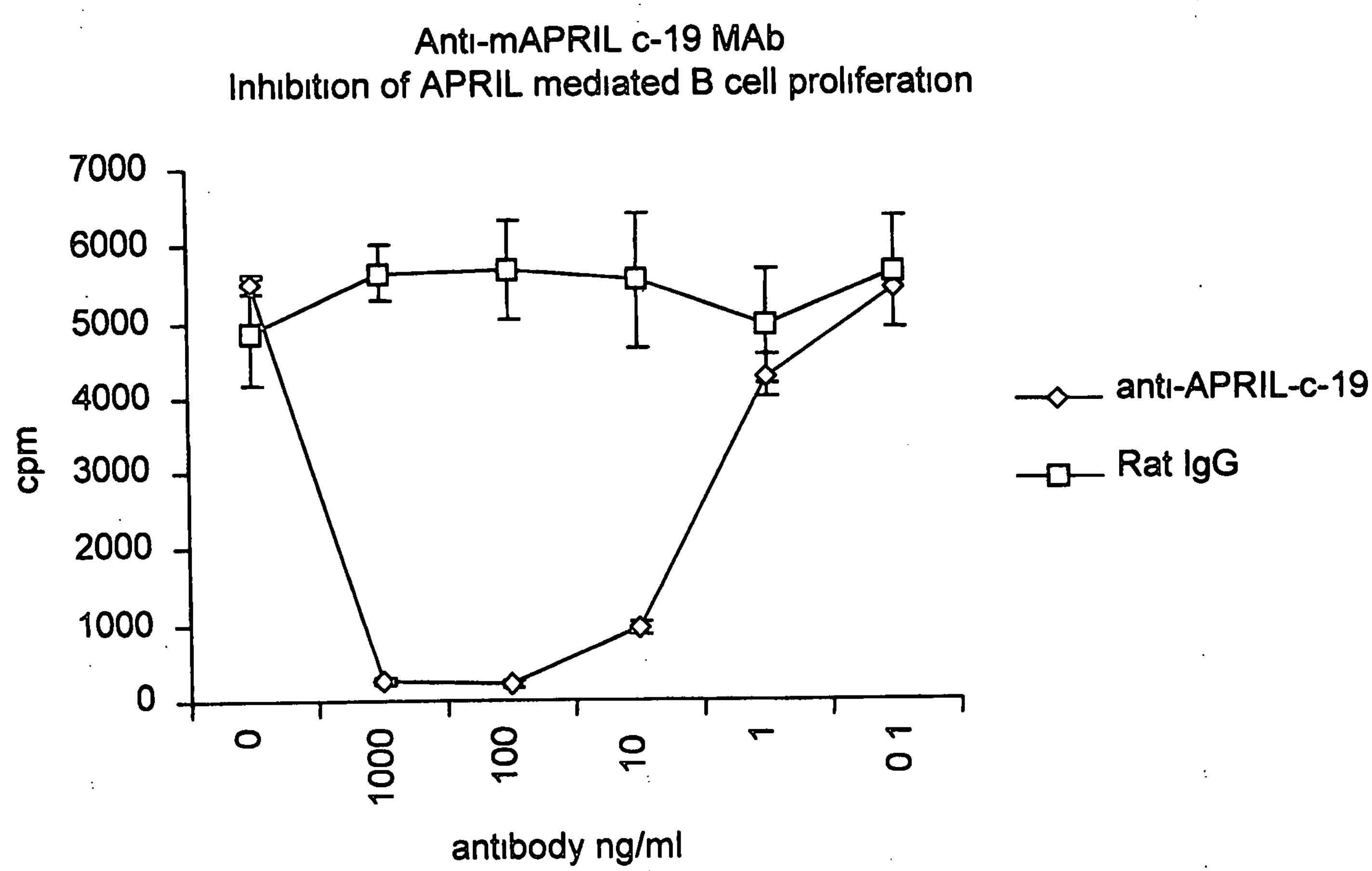


FIG. 30

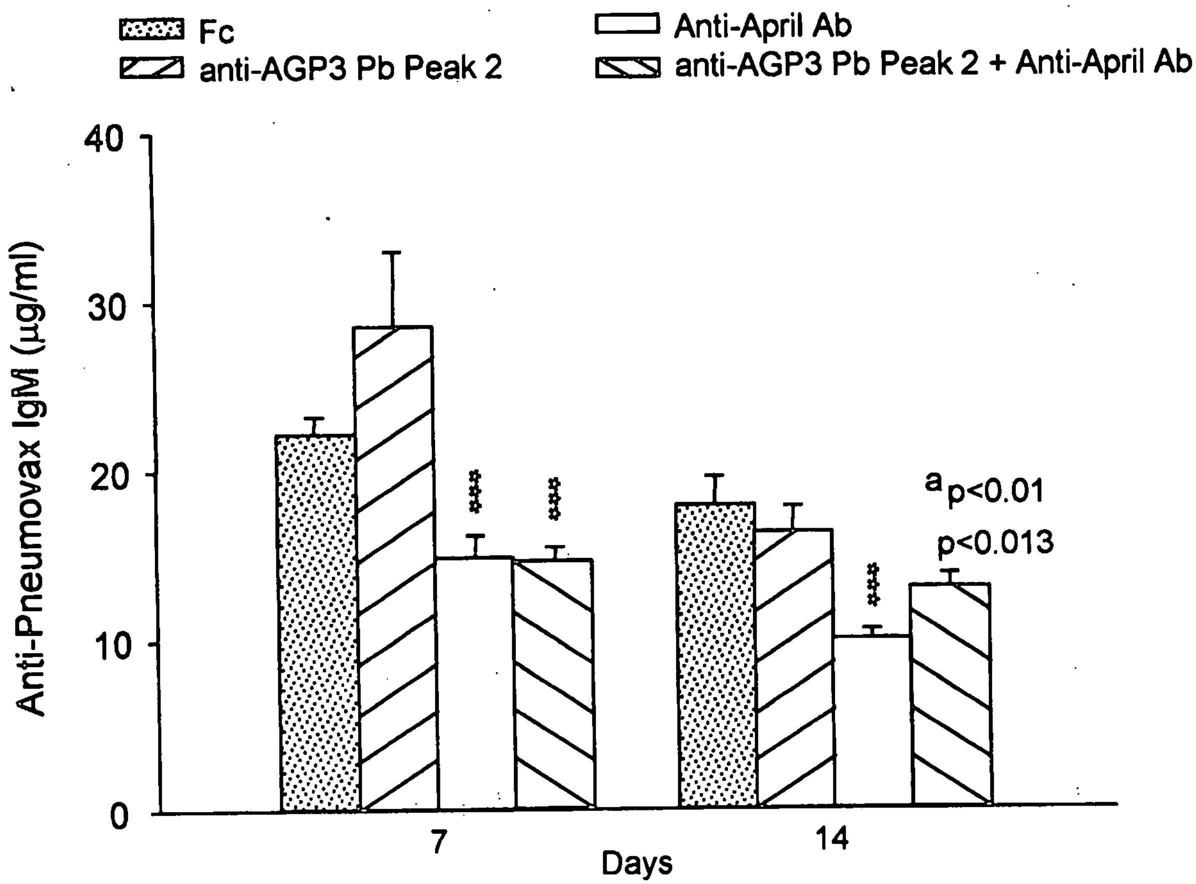


Anti-mAPRIL c-19 MAb
Inhibition of APRIL mediated B cell proliferation
7000
6000
5000
4000
3000
2000
1000
0
cpm
0
1000
100
10
1
0 1
antibody ng/ml
anti-APRIL-c-19
Rat IgG

FIG. 31

Neutralizing anti-mAPRIL Mab Reduces anti-Pheumovacs IgM *In Vivo*

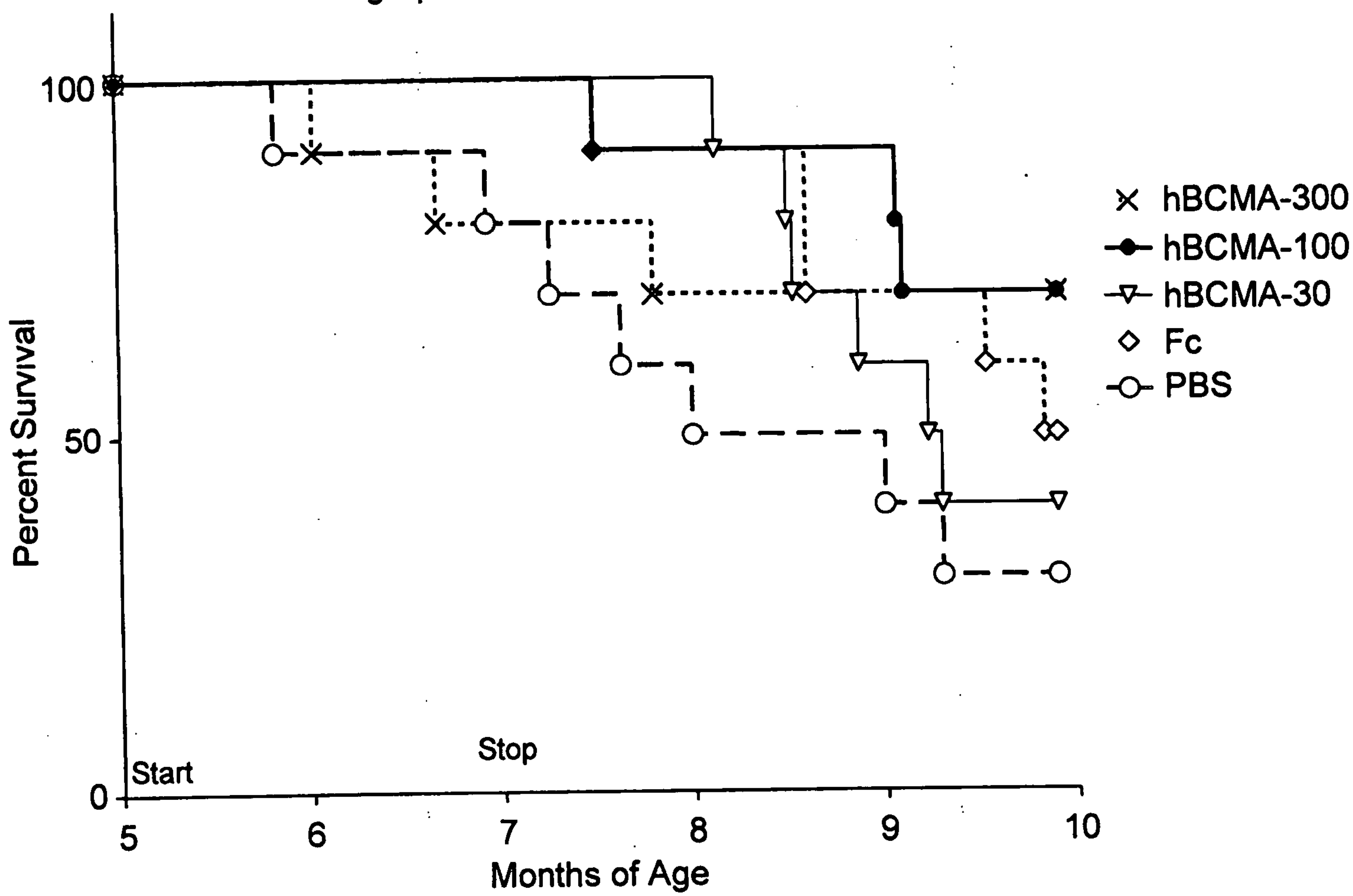
5 mg/kg ip on day 0, 3, and 6



a difference between Anti-April Ab and anti-AGP3 Pb Peak 2+ Anti-April Ab Groups

FIG. 32

Effect of hBCMA-Fc in NCB/NCWF1 mice
Survival graph from various treatment groups

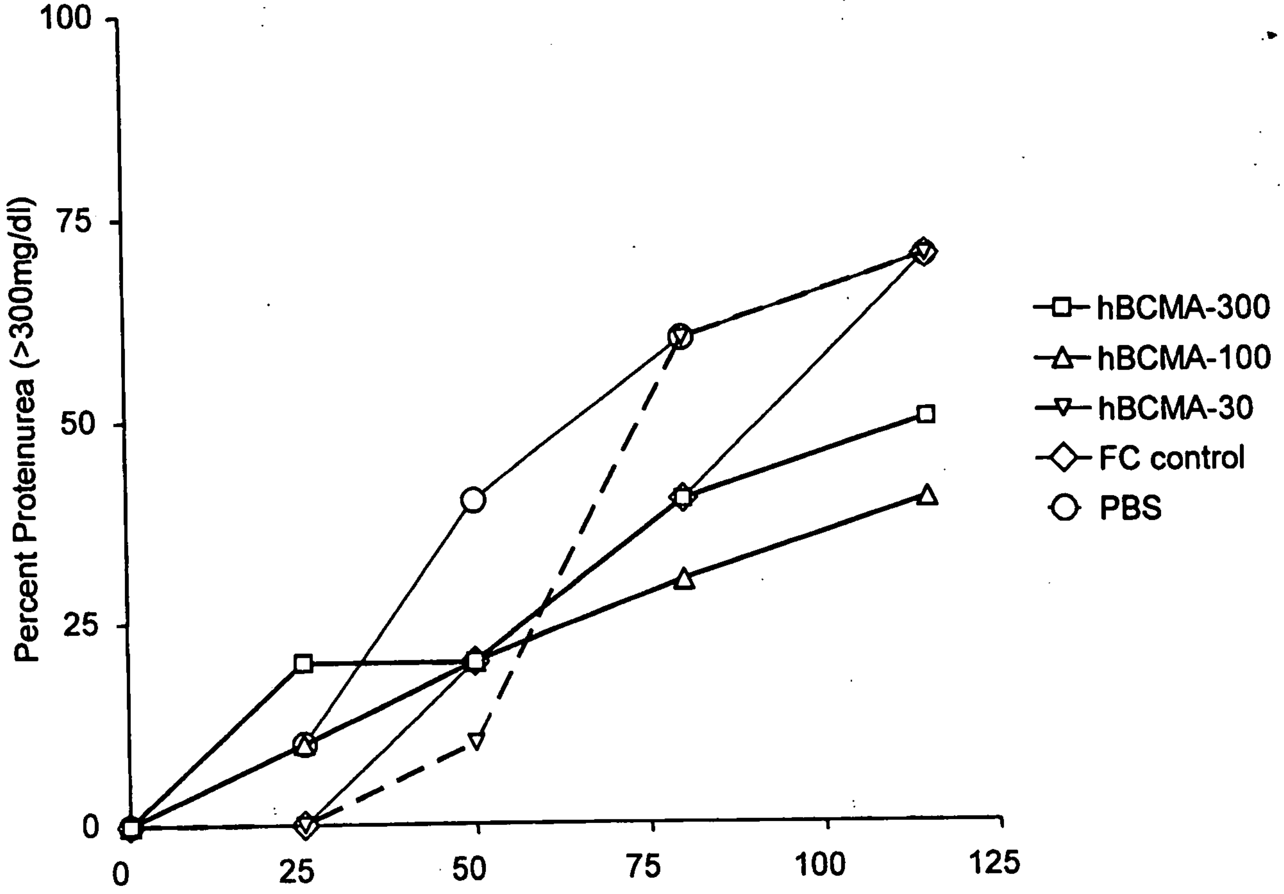


N=10 Mice were treated for 8 weeks 3x/week with the indicated proteins KIN2 group had 12 mice
The 100 in the legend stands for 100 μg of protein or 4mg/kg i p

FIG. 33

Effect of hBCMA-Fc in NCB/NCWF1 mice

Percentage of mice with proteinurea (>300mg/dl) from various treatment groups.



N=10 Five month old BWF1 mice were treated with protein for 8 weeks i p
The hBCMA-300 stands for hBCMA-fc 300 μg/mouse (12mg/kg)

FIG. 34

Analysis of antibodies to dsDNA from the peripheral blood from various treatment groups of BWF1 at day 0,30,60, and 90

MEAN anti-dsDNA isotypes in U/ml

	Day 0		Day 30		Day 60		Day 90	
Group #	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM
hBCMA-300	179	560	163	371	150	706	171	841
hBCMA-100	150	430	259	718	171	822	339	1031
hBCMA-30	377	592	297	458	401	664	424	601
FC	149	371	234	283	384	331	432	351
PBS	308	292	439	311	247	576	720	467

Standard Deviation of the above means

	Day 0		Day 30		Day 60		Day 90	
Group #	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM
hBCMA-300	104	303	116	211	62	518	62	734
hBCMA-100	109	262	306	461	212	758	371	1225
hBCMA-30	363	455	281	430	305	606	421	400
FC	68	160	150	93	391	151	233	237
PBS	311	73	474	152	247	370	870	327

FIG. 35

Evaluation of B cell numbers at treatment day 60 from the12mg/kg (30 ug), 4mg/kg (100ug), and 1 3mg/kg (300 ug) dose of hBCMA-Fc groups along with the Fc and PBS control groups

hBCMA-fc-300

Mouse#	%CD4	%CD8	%B220
1 0	16 3	11 0	16 4
2 0	24 1	11 1	11 6
3 0	18 2	7 4	9 9
4 0	25 4	13 3	13 1
x	21 0	10 7	12 8
sd	4 4	2 4	2 8

hBCMA-100

	%CD4	%CD8	%B220
5 0	26 1	14 9	10 1
6 0	21 1	11 3	10 6
7 0	24 6	13 3	8 3
8 0	20 0	11 3	13 4
x	23 0	12 7	10 6
sd	2 9	1 7	2 1

hBCMA-FC-30

	%CD4	%CD8	%B220
9 0	2 5	6 9	10 3
10 0	13 2	5 2	23 4
11 0	15 9	6 4	29 2
12 0	14 8	7 6	31 5
x	11 6	6 5	23 6
sd	6 2	1 0	9 5

Fc

33 0	7 0	8 1	25 4
34 0	10 7	4 9	15 3
35 0	18 9	9 3	21 0
36 0	20 1	11 1	21 0
x	14 2	8 4	20 7
sd	6 4	2 6	4 1

PBS

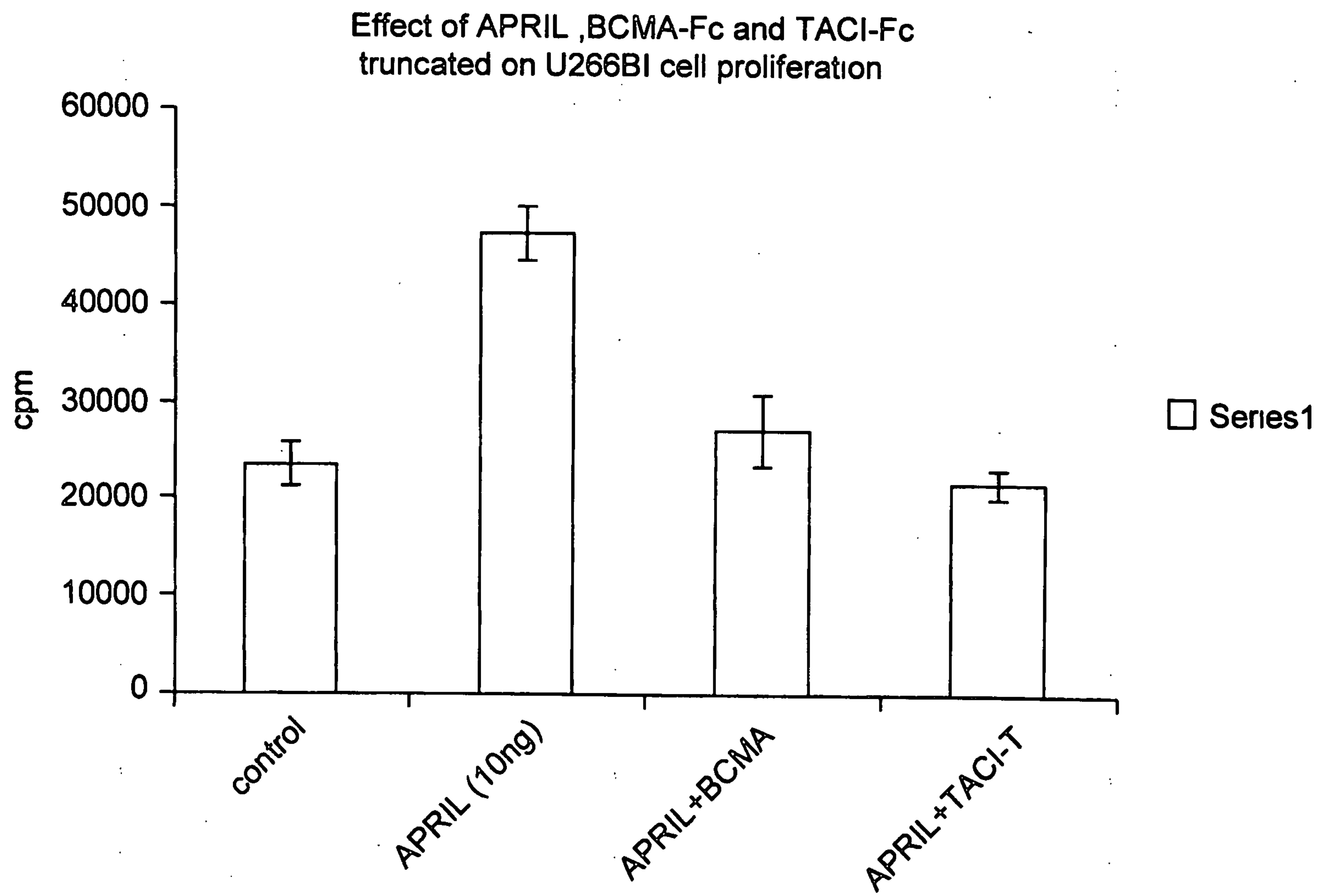
37 0	16 9	8 3	15 5
38 0	19 1	12 1	19 5
39 0	7 1	3 4	17 5
40 0	19 9	11 4	26 5
x	15 8	8 8	19 8
sd	5 9	4 0	4 8

FIG. 36

Specific APRIL binding to Human Cell lines determined by FACS analysis

	APRIL binding
HT 29 Colon adenocarcinoma	+ + +
NCI 460 Lung carcinoma	+ + +
PC3 Prostate adenocarcinoma	+ +
C6 Glial carcinoma	+ +
Raji Burkitt lymphoma	+ + +
A20 Mouse B cell lymphoma	+ + +
U266BI Myeloma	+ + +
A435 Epidermoid carcinoma	--
A469 Kidney carcinoma	--
MDA-231 breast adenocarcinoma	--

FIG. 37



Effect of APRIL ,BCMA-Fc and TACI-Fc truncated on U266BI cell proliferation
cpm
60000
50000
40000
30000
20000
10000
0
control
APRIL (10ng)
APRIL+BCMA
APRIL+TACI-T
Series1

FIG. 38

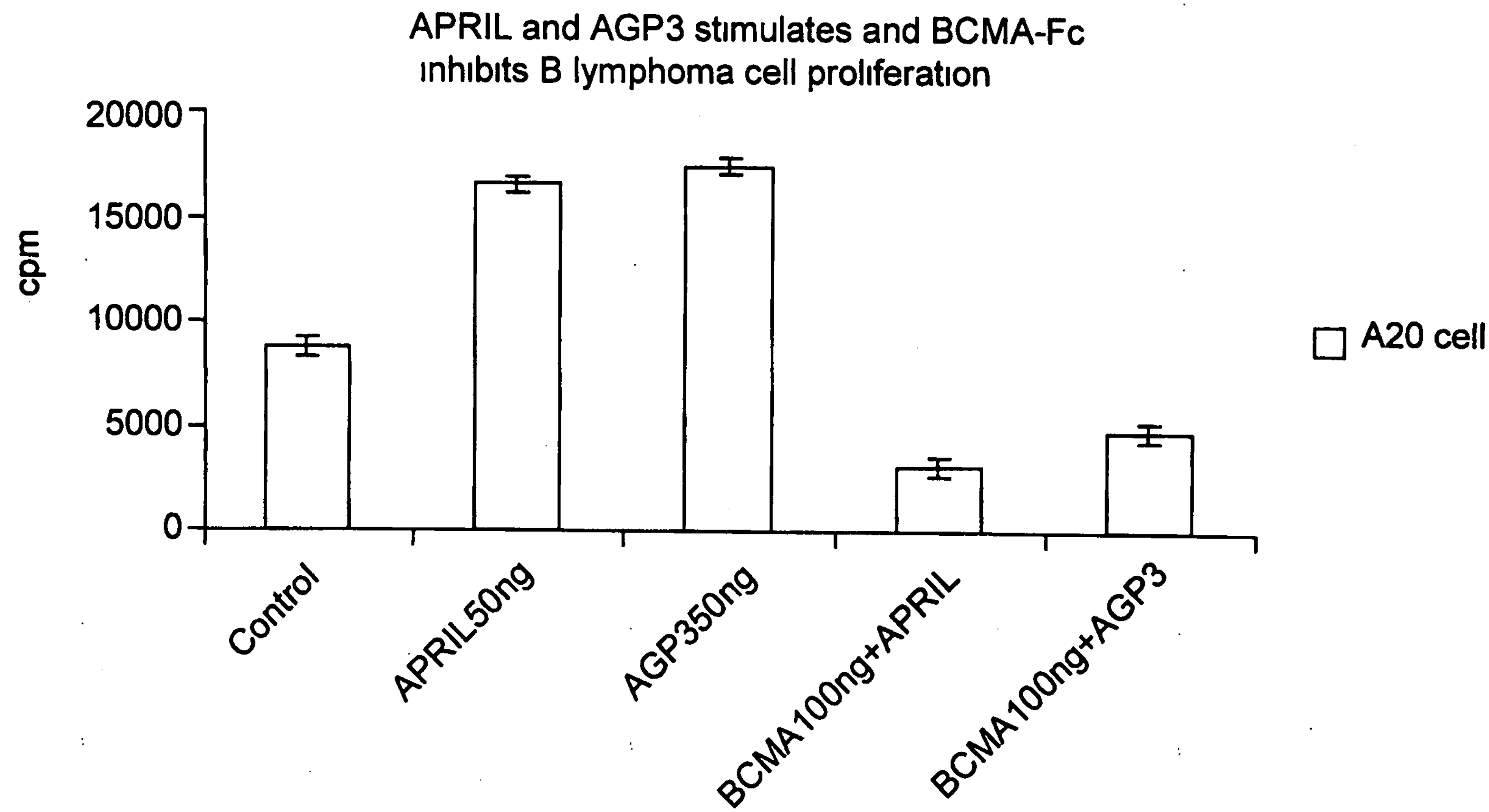

APRIL and AGP3 stimulates and BCMA-Fc inhibits B lymphoma cell proliferation
cpm
20000
15000
10000
5000
0
Control
APRIL50ng
AGP350ng
BCMA100ng+APRIL
BCMA100ng+AGP3
A20 cell

FIG. 39

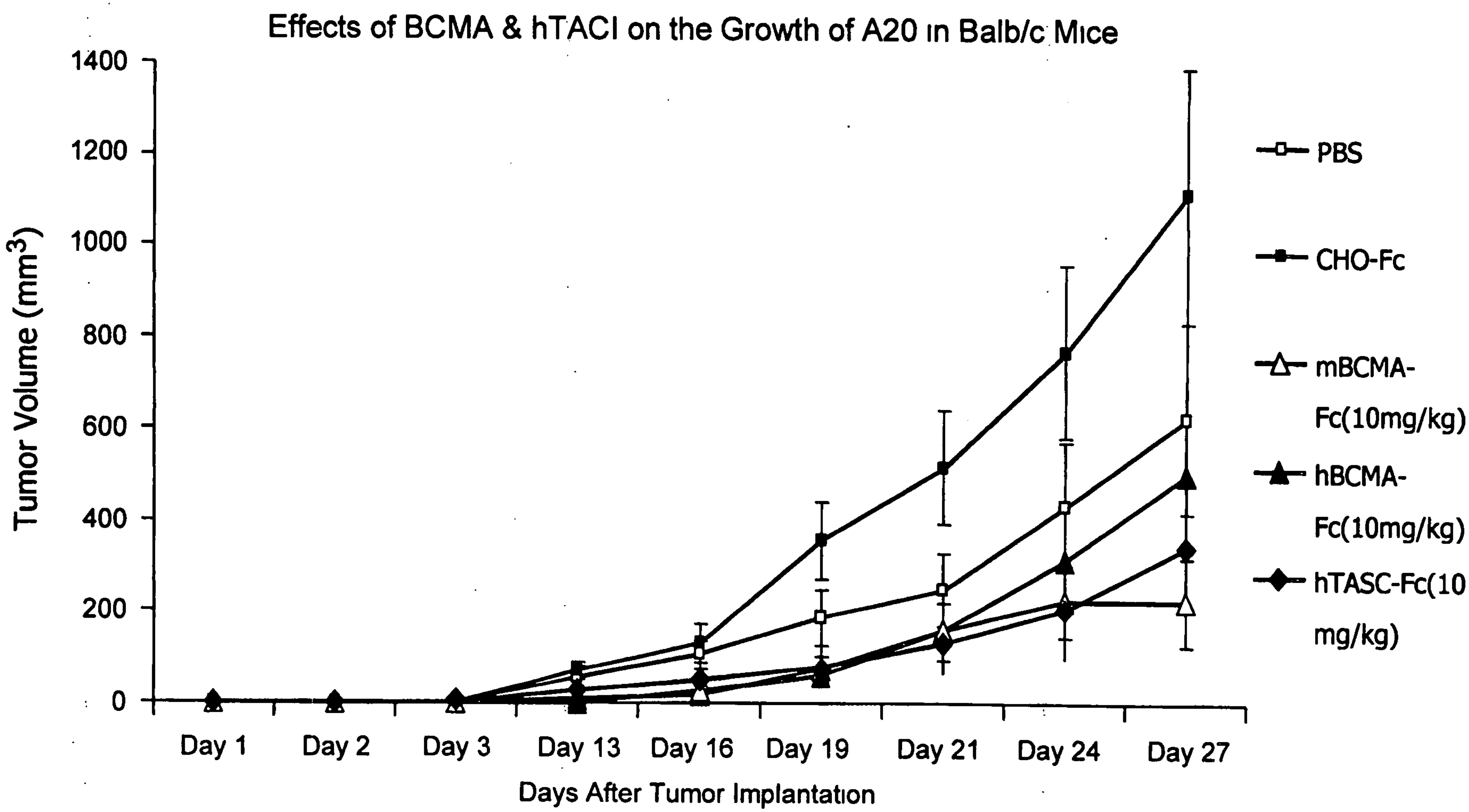
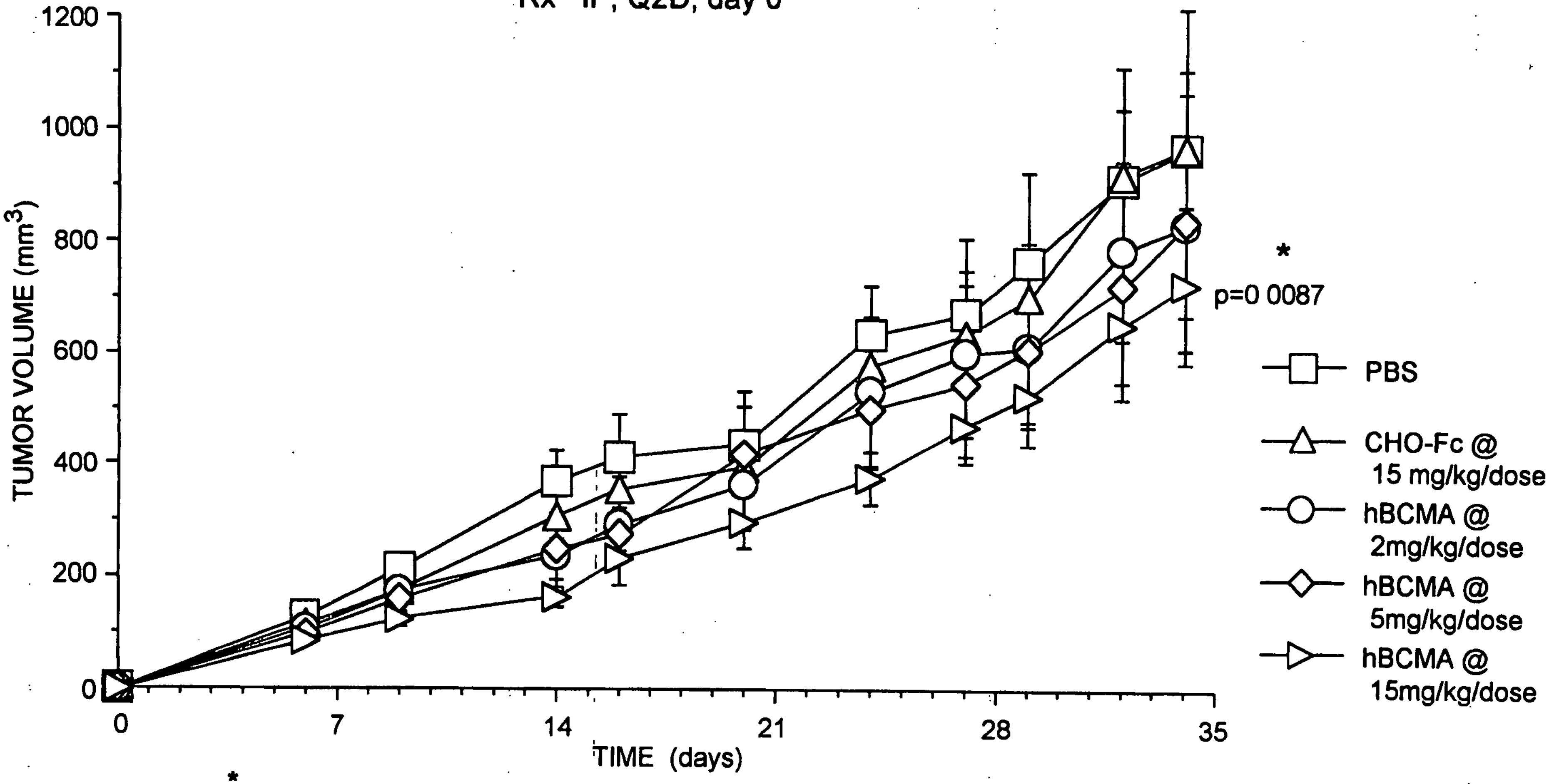

Effects of BCMA & hTACI on the Growth of A20 in Balb/c Mice
Tumor Volume (mm3)
1400
1200
1000
800
600
400
200
0
Day 1
Day 2
Day 3
Day 13
Day 16
Day 19
Day 21
Day 24
Day 27
Days After Tumor Implantation
PBS
CHO-Fc
mBCMA-Fc(10mg/kg)
hBCMA-Fc(10mg/kg)
hTASC-Fc(10 mg/kg)

FIG. 40

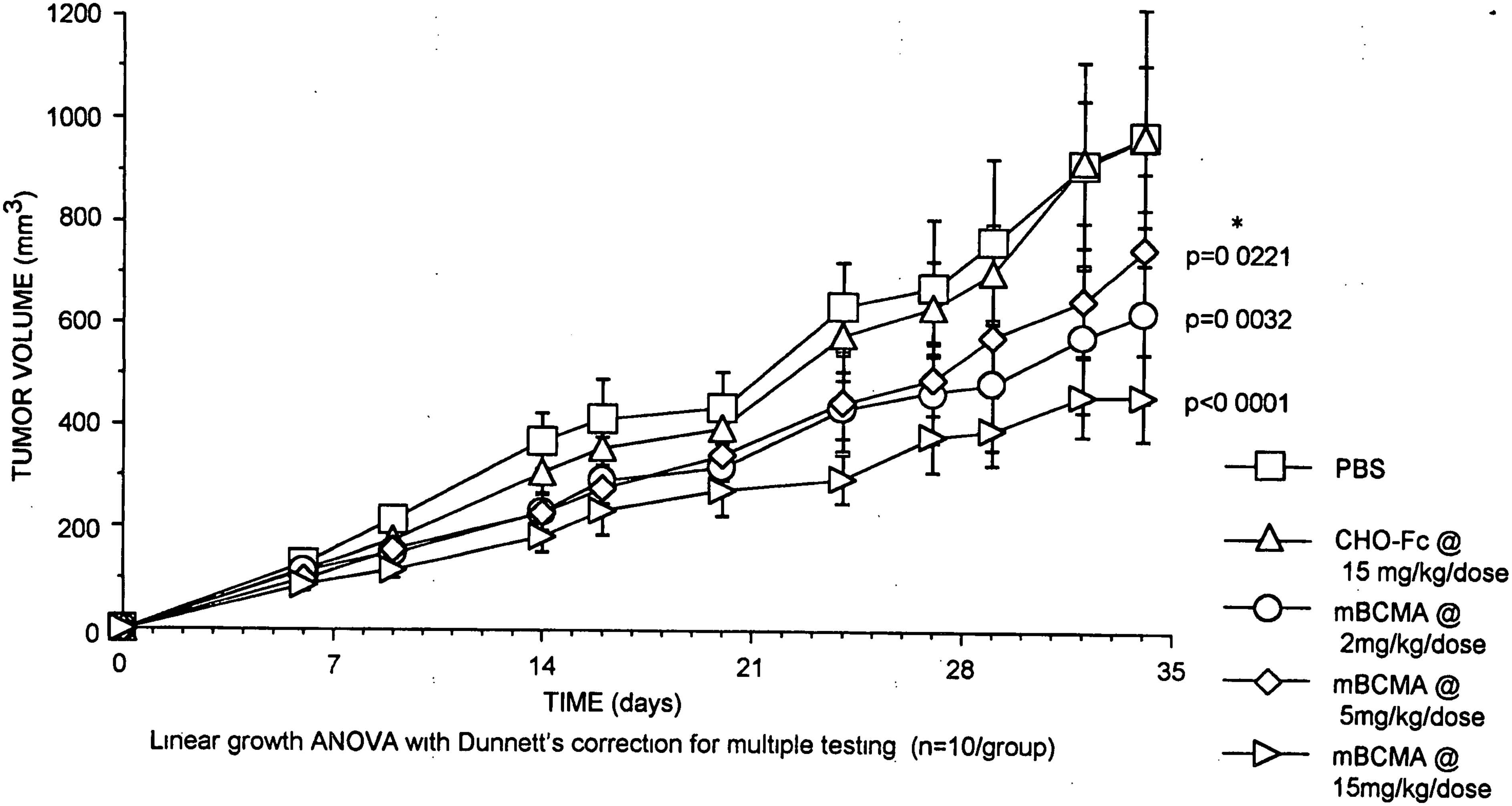
EFFECT OF HUMAN BCMA-Fc AGAINST HT-29 SC TUMOR GROWTH
Rx IP, Q2D, day 0



* Linear growth ANOVA with Dunnett's correction for multiple testing (n=10/group)

FIG. 41

EFFECT OF MURINE BCMA-Fc AGAINST HT-29 SC TUMOR GROWTH
Rx IP, Q2D, day 0



Linear growth ANOVA with Dunnett's correction for multiple testing (n=10/group)